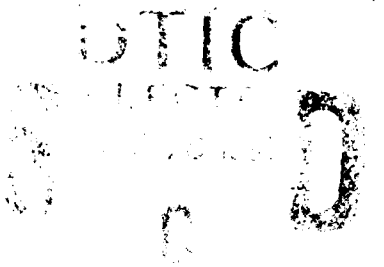

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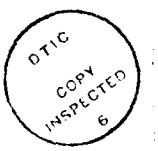

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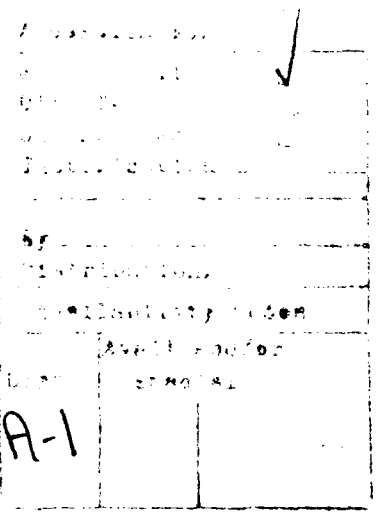

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This report describes progress in a program of research concerned with whether event-related brain potentials (ERPs) provide a reliable, valid, and practical way of predicting performance. Two objectives of the program were to develop the capacity to measure, analyze, and interpret ERPs and to demonstrate that ERPs are sensitive to factors influencing performance. Experiments are described that show ERP variation in studies of orienting responses, habituation, and Pavlovian conditioning. Additional experiments show ERP changes in relation to time-of-day and ultradian variation in performance. Several experiments describe the relationship between ERP and performance changes during the wake/sleep transition. These experiments encourage the view that ERPs are closely related to both arousal and cognitive factors influencing performance.

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FOREWORD

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John Hardy 4-30-91

PI Signature Date

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5.0 INTRODUCTION

THE PROBLEM

Increases in technological sophistication in civilian and military work settings has resulted in greater demands being placed on human operators of man-machine systems. Often, machines respond more quickly than humans and perform a greater number of complex functions. However, such systems require surveillance by alert human monitors. The latter has resulted in a greater need to understand the factors which affect the performance of human monitors and has created a greater need to assess their performance readiness, particularly under conditions that might reduce readiness (e.g. sleep loss fatigue, boredom, hypothermia, hyperthermia, exposure to chemical agents, etc.).

In the past, researchers have used a variety of measures to infer central states related to performance readiness. The measures generally used were blood and urine composition, heart rate, galvanic skin response, electromyography, and others. Inferences based on these measures, however, have been of limited value in predicting and understanding performance changes. One likely reason for the lack of success is that these measures deal with peripheral physiological systems which are too distant from central processes to permit valid inferences. The purpose of the present research is to assess the usefulness of event-related brain potentials (ERPS) which are considered to be more closely related to central processes.

Event-related potentials are brain potentials that can be recorded in response to discrete stimuli. When measured under appropriate conditions, some ERP components are related to the physical characteristics while others are related to the psychological characteristics of stimuli. Recent technological developments have resulted in reliable and efficient procedures for recording, measurement and quantification of this activity.

Evoked potentials have been found to be related to performance on tasks involving stimulus detection, discrimination, and decision making. Further, they are thought to provide neurophysiological correlates of central states such as attention, information processing, and allocation of processing resources.

The research of concern here was about whether ERP measures provide a reliable and practical way of predicting performance changes resulting from the effects of environmental, task, and field conditions. The research was based on an earlier study involving ERPs and sleep deprivation (U.S. Army contract titled Auditory Evoked Potentials as a Function of Sleep Deprivation and Recovery Sleep"). The latter focussed on identifying fundamental relationships that exist between ERP measures, different levels of sleep deprivation and recovery sleep, and performance on several tasks involving psychological functioning and psychomotor performance. Sleep deprivation was chosen as a laboratory manipulation because: 1) previous research indicated that evoked potentials change with sleep and sleepiness (e.g., Gauthier & Gottesman, 1983); 2) it is an important, yet simple variable to

quantify and to vary systematically; 3) it enters into relationships with many other variables; 4) it has high inherent interest in military and civilian work settings (e.g., Naitoh & Townsend, 1970).

RESULTS OF PREVIOUS WORK

We found several interesting relationships in the research conducted under our first U.S. Army contract. These relationships over 48-hrs of sleep deprivation can be summarized as follows: 1) sleep deprivation results in performance degradation; 2) the degradation in performance is marked by circadian effects; 3) sleep deprivation also has a marked effect on cortical evoked response measures 4) the circadian variation is also apparent in the cortical evoked responses recorded during the deprivation period); 5) later (N200, P300) components of evoked responses covary with changes in performance associated with sleep deprivation and circadian variation; 6) earlier (P100, N100, P200) evoked potential components covary with individual differences in performance throughout the deprivation period; and 7) the predictive relationships between ERPs and performance appear stronger for tasks involving a rate measure than for tasks not involving a rate measure.

One reason that our earlier findings are potentially important for prediction of changes in performance is that some of the relationships involved N200 deflection of the evoked potential. N200 can be recorded with minimal intrusion. The sensitivity of P300, for example, depends on subjects carefully attending to the eliciting stimulus, N200 may not. Thus N200 across sleep deprivation conditions may be a particularly useful predictor of performance degradation.

Another reason why the findings may be important is that N100, P300, and N200 correlated with individual differences in performance. This finding adds to the evidence that evoked potentials provide a basis for classification/selection of individuals in some performance settings (cf. Lewis, 1983; Wilson & O'Donnell, 1986).

A further reason that the results may be important relates to the finding that the evoked potentials were more clearly related to the performance measures involving rate as a response dimension. ERP measures may be selectively related to the attentional, perceptual, and processing activities underlying rate measures of performance. It is particularly important that a better understanding of this relationship be developed so that the usefulness of evoked potentials in predicting performance degradation can be assessed.

PROPOSED WORK

The research proposed under our current contract was concerned with the replication and extension of the findings of our initial experiment. The goals were: 1) to replicate and extend the findings noted above and assess the extent to which ERPs can be used to provide a greater understanding of the attentional, perceptual, and processing changes underlying performance degradation in a stressful environment; 2) to develop

a predictive model (see below) between the different components of evoked responses and performance degradation; 3) to identify the maximum lead-time in which evoked responses may predict performance changes; 4) to assess ways of enhancing the relationship between changes in evoked responses and changes in performance; 5) to evaluate techniques used by others to measure central nervous system activity; and 6) to assess the extent to which evoked responses can be used to identify those individuals who will perform well on selected tasks from those who will not perform well.

RESEARCH PLAN

The plan described for achieving the goals included a three-phase program. During Phase I (Year 1), the general objectives were to develop further our capability to measure, analyze, and interpret event-related potentials and to refine our existing battery of performance measures. The objectives of Phase II (Year 2) were to replicate and extend our earlier findings and demonstrate that evoked-response measures are at least as sensitive to conditions degrading performance as more conventional measures. Phase III objectives were to examine correspondence between ERPs and performance during long-term sleep deprivation.

RESEARCH PROGRESS

Software Development. Considerable progress in achieving the goals described above was made. A major accomplishment for our laboratories was the development of software for the organization, display, and evaluation of ERPs. This program called "EVAL" is unique in the research community in that it was written for a PC rather than a main frame computer. It offers the ability to filter, correct for artifact, and display and analyze data on a sweep-by-sweep or averaged basis.

Research. Several experiments were completed. The section below describes these experiments.

6.0 BODY

6.1 Experiment 1 - Habituation of the P300 to Target Stimuli: Are Arousal and Attention Factors?

This research focusses on the decrement in amplitude of the P300 to target stimuli under conditions of repeated testing (i.e., habituation). It is generally assumed that the P300 to task-related stimuli (targets) does not habituate even though habituation to non-task related stimuli (non-targets) occurs rapidly (e.g., Courchesne, Courchesne, & Hillyard, 1978; Megela & Tyler, 1979). However, recent findings have revealed that a decrement in P300 amplitude to targets can also occur (Wesensten, Badia, & Harsh, 1991). The findings regarding targets found a 40% decrement in P300 amplitude with repeated testing. Why and under what conditions does this P300 index of cognitive processing habituate?

Experiment 1a provides a detailed assessment of P300 habituation and dishabituation (recovery). Several conditions under which dishabituation might occur were examined. The latter were chosen based on studies (e.g., Badia & DeFran, 1970; Thompson & Spencer, 1966) showing habituation and dishabituation using other response measures (i.e., skin conductance response [SCR]). It was assumed that conditions resulting in recovery of the SCR will affect the P300 in a similar manner. Thus, for one condition of Experiment 1a we introduced a stimulus change during testing to determine whether an habituated P300 will recover. For a second condition, the incentive effect of information was assessed. There are data which indicate that giving subjects information about when the experimental session is nearing an end results in enhanced performance (Haslam, 1983).

Experiment 1a

A standard oddball paradigm was used and we focussed on the pattern of habituation across blocks of 35 targets. Following five blocks of testing, four conditions were imposed: a) Group 1, no change; b) Group 2, reversal of target and non-target tones; c) Group 3, information (Knowledge) that the last block of testing was to occur; d) Group 4, both b and c.

Method

Subjects and Procedure Forty subjects (freshman college students, 10 male, 30 female) were assigned randomly to the four conditions. Evoked potentials were recorded using Grass amplifiers and electrodes. Tones were presented via headphones at 80 dB SPL. Probability of targets (1200 Hz) was 0.2, whereas probability of non-targets (1000 Hz) was 0.80. The interstimulus interval was 1500 ms, digitizing was at 280 Hz with a signal averaging window of 810 ms. Six blocks of testing were given, each containing 35 targets and about 160 non-targets. The interblock interval was 20 s. The first 5 blocks were identical for all subjects and the treatment was introduced on Block 6.

Results

Habituation Figure 1 shows the diminution in P300 amplitude across Blocks 1-5. The decrease becomes very apparent when comparisons are made between Block 1 and Block 5; amplitude decreased from 11.3 uV on Block 1 to 5.4 uV on Block 5. Statistical analysis revealed that the main effect for Block was significant, $F(4,144)=22.7$, $p<.01$. The analysis of P300 latency revealed the same effect in that latencies increased significantly ($p<.01$).

Treatment Effects (Dishabituation) Figure 1 also shows the change in amplitude (recovery) from Block 5 to Block 6 for the four conditions. A significant main effect for Groups was found, $F(3,36)=5.4$, $p<.05$. As shown, a substantial increase in P300 amplitude occurred only for the Knowledge Group and the Knowledge & Reversal Group. The Reversal Group did not differ from the Control group.

Within Block Analysis Figure 2 depicts the data of the "Knowledge" groups somewhat differently. For Figure 2 each of the 7 points within a block represents an average across 5 targets instead of across 35 targets as shown earlier. The total number of targets and non-targets remain the same. One advantage of averaging over blocks of 5 targets is that it permits one to observe changes that may occur within the larger block of 35 targets. The amplitudes at the beginning of each block were generally higher and then show a decrease within a block. Each block shows the same pattern: amplitude recovery at the beginning of the block followed immediately by a diminution in amplitude for the remainder of the block. This sub-blocks analysis was statistically significant ($p<.05$).

Discussion

Both habituation and dishabituation of P300 amplitude were clearly documented. Two conditions gave rise to dishabituation. One was the treatment condition of "Knowledge" and the other was the interblock interval (Within Block analysis). Both may be related. Why are the amplitudes higher at the beginning of a block? Why do they then decrease? Several events occurred between blocks. During this time the participant was asked the number of targets presented. Their answers were generally very accurate. After a moment to relax they were instructed that another series of tones was to begin and that they should again count the targets and press the switch. These events may have refocussed them on the task and may have been responsible for the increase in amplitude at the beginning of each block. Post experimental interviews provided some support for the latter. Subjects reported that the task was very easy, required little effort, and that it was very boring. They reported being more into the task at the beginning of the block. As stimuli continued to be presented, however, other factors began to exert an effect. Subjects reported growing bored, drowsy and thoughts unrelated to the task intruded and increased in frequency.

How do we interpret these observations? Is the reduction in amplitude across blocks due to a reduction in attention to the

target task, i.e., intrusion of competing thoughts? In effect, subjects were performing two concurrent tasks--the target task and unrelated intrusive thoughts. There are data showing that requiring a concurrent task (mental arithmetic, tracking a different target) while instructed to count targets results in a decrease in P300 amplitude. Another factor affecting P300 amplitude could be arousal level. Could the decrease in amplitude be related to a decrease in arousal/alertness? Subjects did report being very bored and, at times, drowsy. We know that arousal level can have powerful effects. For example, in sleep deprivation studies of 48 to 72 hours, performance deteriorates considerably. However, if subjects are informed that the deprivation period is about to end subjects are aroused and performance level makes a remarkable recovery.

Obviously habituation was reversed by the information condition. However, these findings are compatible with both the "arousal" interpretation and the "attention" interpretation. One or both factors may be important. Our subjects reported higher arousal/alertness after being given the "end-of-session" information and also being more attentive to the task because they knew that it was their last effort. Thus, an increase in general arousal and an increase in attention to the task occurred for the knowledge groups. We attempted to separate these two factors in our next experiment.

Experiment 1b

For our next study we measured arousal levels using tonic skin conductance level (SCL) as the measure. Our interest was in contrasting an interpretation focussing on arousal with an interpretation focussing on attention to the task. Again, the oddball task was used. Six blocks of testing were given and SCLs were measured from the first block to the end of the sixth block. We assumed that the greater the SCL, the higher the arousal level.

Method

Subjects and Procedure Twenty undergraduate female subjects were assigned randomly to two groups. The first three blocks were the same for all groups and the treatment was introduced at the beginning of Block 4. Thus, we expected that P300 amplitude would show a decrease across the first three blocks (i.e., habituation). We assessed whether arousal also declined. For Group 1, subjects were instructed at the beginning of Blocks 4, 5, and 6 to "Stand" upright from their sitting position for a few seconds ("Stand" condition) and to stretch fully. We assumed that doing so would combat any drowsiness and boredom and would increase arousal level as indexed by the SCL. Group 2 subjects were instructed not only to "Stand" and "Stretch", but they were also informed that they would receive, at the end of each block, $1.00 for correct responding. We assumed that money would focus their attention on the task.

Results and Discussion

Figure 3 shows the results of these manipulations. The decrease in P300 amplitude across the first 3 blocks

(habituation) was significant, $F(2,38)=18.2$, $p<.01$. Figure 3 also shows that tonic skin conductance levels dropped sharply $F(2,38)=31.8$, $p<.01$) over Blocks 1-3 and that this occurred about equally for both groups ($F<1$). On Block 4 the treatment conditions were introduced. Again, it is clear that arousal (tonic SC levels) increased to similar levels for both conditions across Blocks 4, 5, and 6 ($F<1$) yet only the "attention" condition was effective in increasing P300 amplitudes (dishabituation). Obviously since SCL was essentially the same for both conditions, simply increasing arousal level in itself was not a sufficient condition for increasing the amplitude of the P300.

These data support "attention to the task" as an important factor concerning P300 amplitude. If one assumes that the incentive condition focussed the subjects attention on the task, then the waxing and waning of attention may be the major factor affecting increases or decreases in P300 amplitudes. That attention can wax and wane in an oddball task and not be reflected in the accuracy of counting or responding to targets is surprising. An attention interpretation fits well with the data presented in Figure 3 showing a recovery of P300 amplitude between blocks and a slow diminution in amplitude within a block of 35 targets. The gradual decrement between blocks is presumably due to the "waning of attention" across time. The repeat of instructions prior to each new block focussed attention on the task, though briefly, and resulted in higher amplitudes at the beginning of each block. Knowledge concerning the "end of session" and the incentive of money also focussed attention on the task. Thus, it appears that it is not the cognitive process indexed by the P300 that attenuates across blocks of testing, it is the failure of the task to invoke the process that results in attenuation of P300 amplitude.

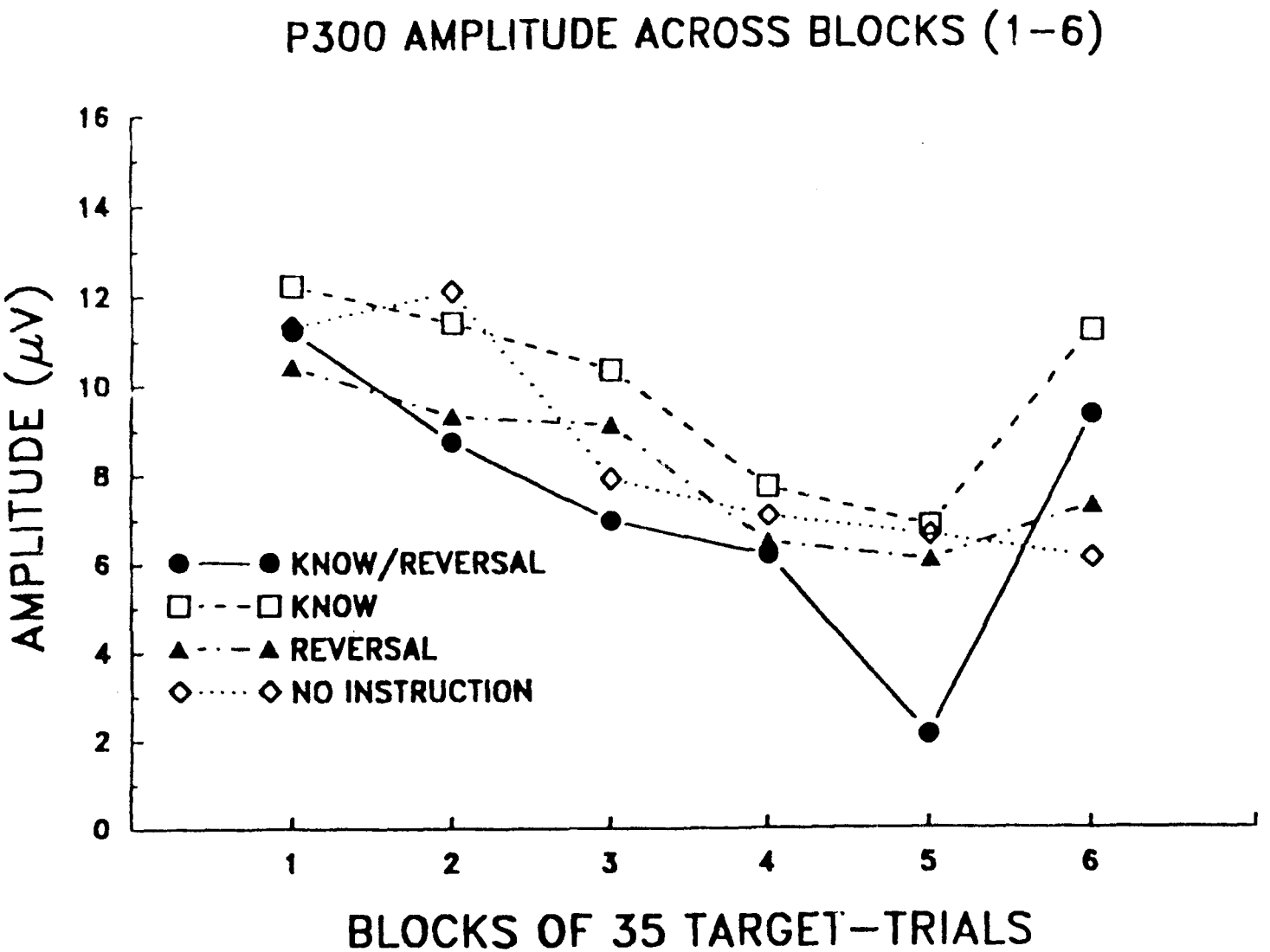


Figure 1. Mean P300 amplitudes across blocks for the four experimental conditions.

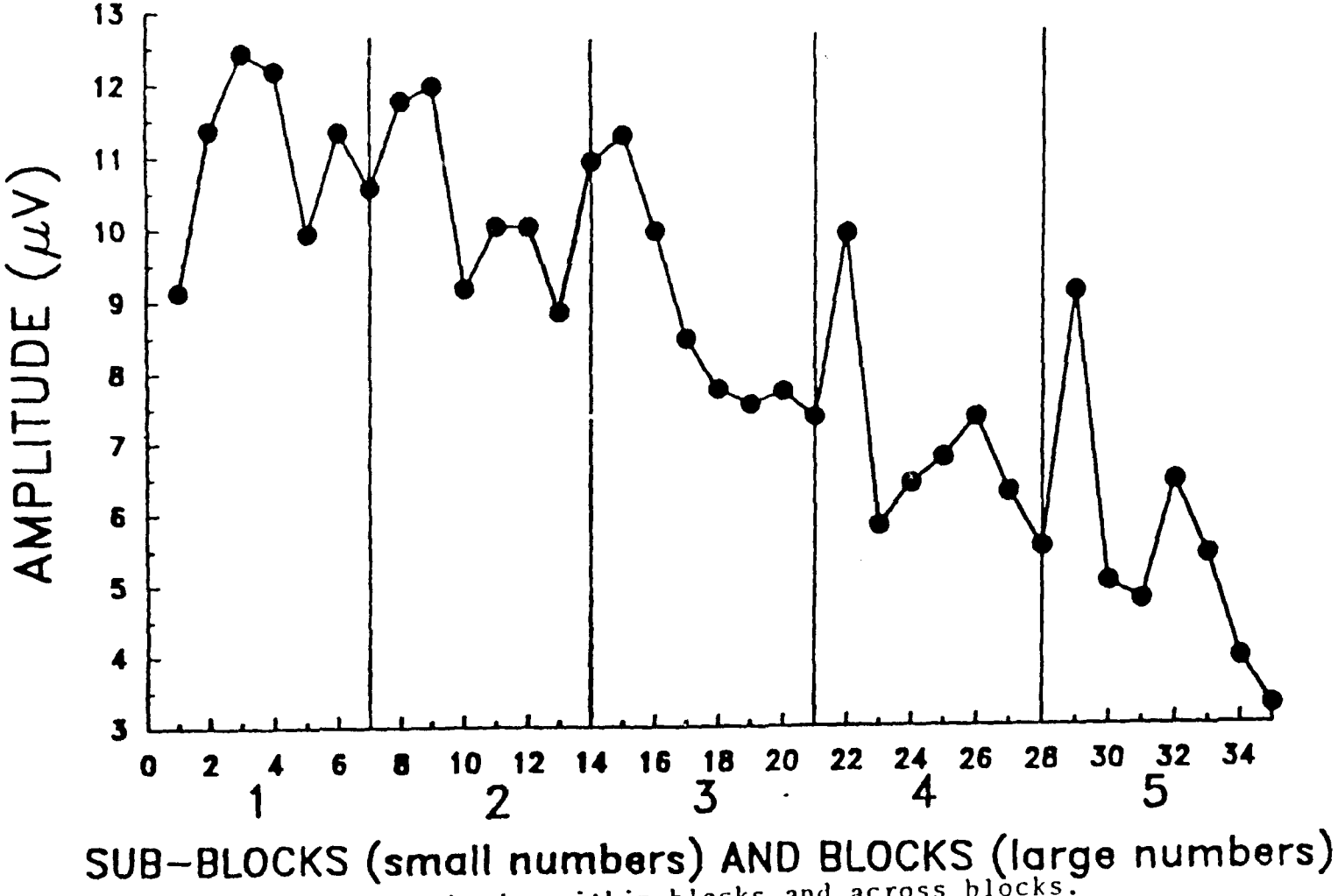
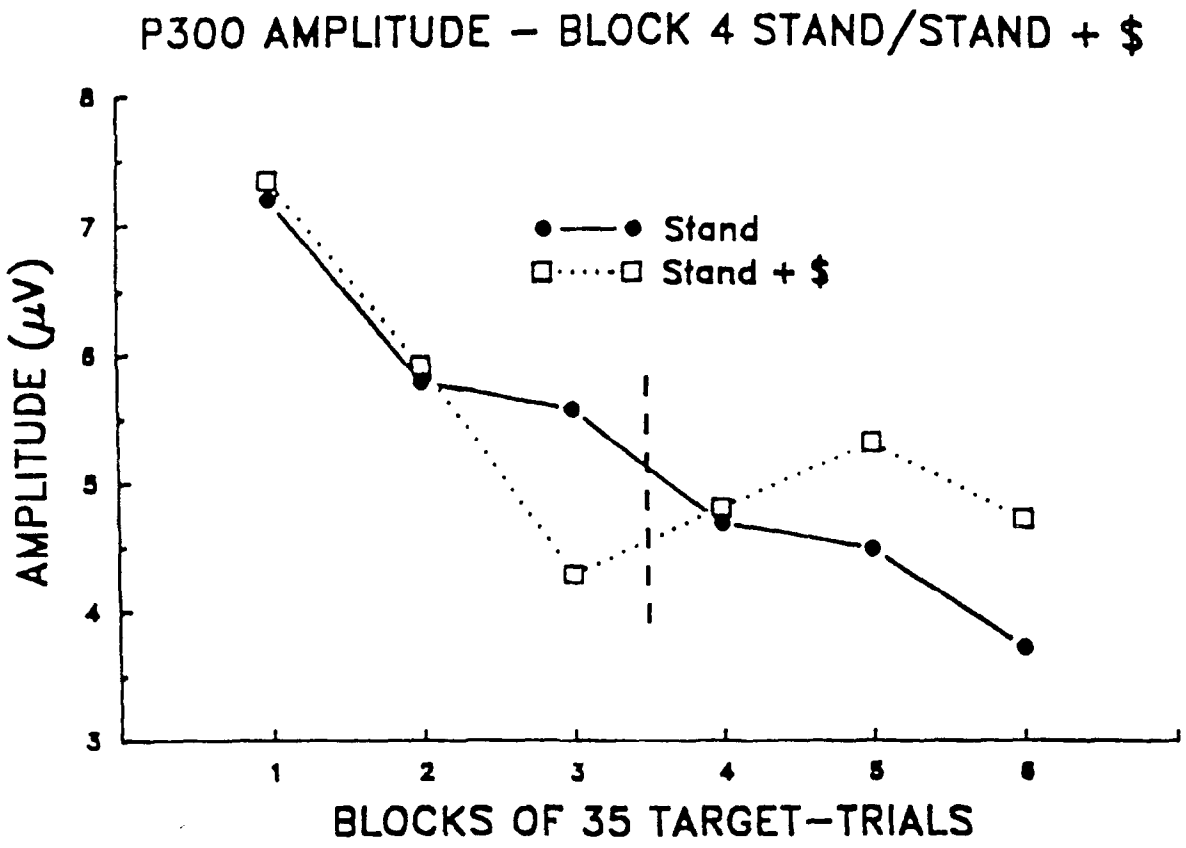


Figure 2. P300 amplitudes within blocks and across blocks. Each block of 35 targets is shown in sub-blocks of 5 targets.



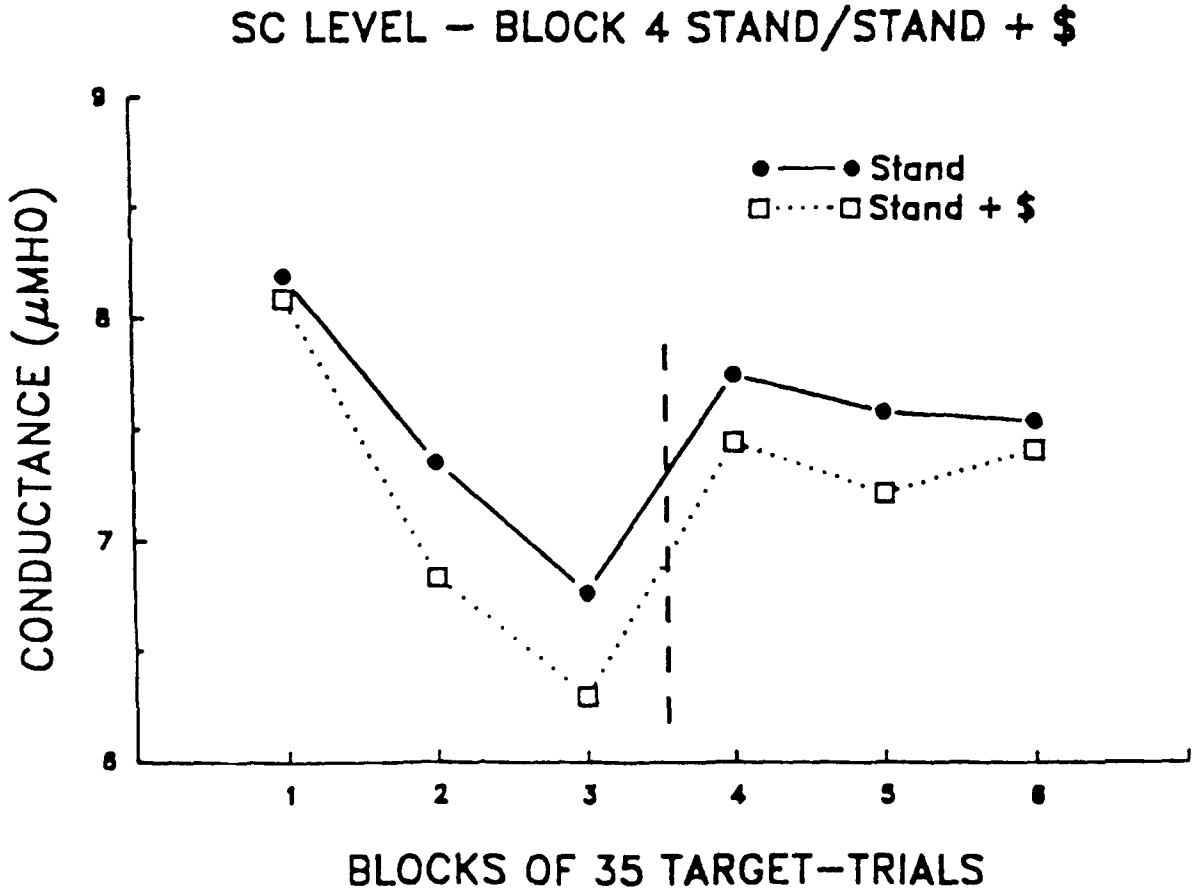


Figure 5. P300 amplitude and tonic skin conductance level prior to and following the treatment condition.

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6.2 Experiment 2 - Orienting Responses and Event-Related Brain Potentials

Research on the orienting response (OR) has traditionally involved responses controlled by the peripheral autonomic nervous system (Thompson & Spencer, 1966). Thus, our understanding of OR mechanisms and their relationship to conditioning, learning, information processing, etc. is based on effector organ responses and the neural processes mediating those responses. Recently, efforts have been made to assess orienting in terms of central measures such as event related brain potentials (Donchin et al., 1984). So called endogenous components of evoked brain potentials have properties in common with the orienting response. Importantly, both share the property of stimulus nonspecificity. That is, they are both evoked by stimulation of a variety of types and quality and both may occur when an expected stimulus is omitted.

Additionally, there are similarities in the eliciting conditions of orienting responses and the endogenous components of ERPs. Figures 1 and 2 illustrate an SCR, an event related brain potential, and the stimulus determinants of the two responses.

On the left side of Figure 1 is a schematic of a skin conductance response. This response is probably the most widely used and validated measure of the orienting response. Our focus here will be on SCR amplitude which is generally conductance at the peak minus conductance prior to the response. On the right side of Figure 1 is a list of the major stimulus factors related to SCR amplitude. Thus an SCR will vary in relation to stimulus novelty, i.e., the extent to which it deviates from expectations regarding its probability, modality, or timing; stimulus meaning, e.g., whether it is or is not a signal stimulus, or relevant or irrelevant to the subjects; and stimulus salience, for ex., its intensity.

On the left side of Figure 2 is a schematic of an event related potential. Event-related potentials -- ERPs, are measured from electrode placements at various locations on the scalp and several different components are typically identified. The focus here is on the positive going component at usually 300 or more ms post stimulus. The amplitude of this P300 component is generally measured in relation to a prestimulus baseline. On the right side of Figure 2 is a list of the major stimulus factors associated with P300 amplitude. Again, novelty, meaning, and salience are important. Thus, the eliciting conditions for the SCR and P300 are at least to a substantial degree, identical.

The fact that the SCR and the P300 have the same eliciting conditions does not necessarily mean that peripheral and central measures can be used interchangeably as indices of the orienting response. There are additional and fundamental properties of orienting responses that may or may not be shared by evoked potentials. For example, with repeated stimulation, orienting responses decline -- they are said to habituate. P300 in many

studies, however, looks the same across many hundreds of stimulus presentations -- there is no evidence of habituation. Another property associated with orienting responses is dishabituation, i.e., recovery of a habituated response following presentation of a test stimulus whose properties differ from the habituating stimulus. Dishabituation of ERPs has received little attention.

Unfortunately, comparisons of the properties of orienting responses and evoked potentials are severely limited by the differences in paradigms and analytic strategies used in their investigation. Figure 3 illustrates some of these differences

One way of assessing whether ERP responses have the same properties as ORs requires study of ERPs using OR paradigms. Thus, ERPs need to be studied with longer ISIs, with nonsignal stimuli, and with procedures that provide for a finer-grained analysis of time effects. There are a handful of studies that have taken this approach.

Another way of assessing whether ERP responses have the same properties a ORs involves including traditional orienting response measures in studies using the ERP paradigm. This was the approach taken in the present experiment.

Method

An "oddball task" was used where subjects were presented target and nontarget tones (90 dB, 1.0 and 1.5 KH tones). The subjects were instructed to tap their foot when targets were detected and to keep count of the number of target stimuli presented. They were asked to ignore the nontarget stimuli. The stimuli were equiprobable. Both ERPs and SCR were recorded to 35 target and 35 nontarget stimuli. To assess dishabituation, a 4 KHz tone was presented between trials 30 and 31.

Results

Figure 3 presents the SCR averaged for seven blocks of five trials. As expected, amplitude decreased across the first six blocks. Although target amplitude was higher on block 1, there was no significant differences in overall level or rate of habituation for the target and nontarget stimuli. Unexpectedly there were no signs of dishabituation during the seventh trial block.

Figure 4 presents the SCR data across six blocks of two trials (data from the first 12 trials). Differences are apparent here on the very first block, but not on subsequent blocks.

With regard to SCR then, we found 1) habituation of the SCR response to both signal and nonsignal stimuli, 2) evidence of a larger initial (first two trials) response to the signal (target) stimulus, and 3) no sign of dishabituation.

Figure 5 (top) presents the P300 data for seven blocks of five trials. The plotted data points at each block are a percentage of the first trial block for target and nontarget stimuli. Overall the amplitude of the target P300 was nonsignificantly larger than the nontarget P300. Data from the Fz lead only are presented. No significant differences were found at Cz and Pz.

It can be seen that the rate of habituation was greater for

the target than the nontarget tone. The decrease for the nontarget tone was not statistically significant.

Dishabituation can also be seen. Relative to block six, the magnitude of the response was greater following the dishabituation stimulus for both tones (significantly greater for the target but not the nontarget).

Figure 5 (bottom) also presents the ERP responses across six blocks of two trials (the first 12 trials). Again there is clear evidence of habituation with the target but not the nontarget stimulus. It appears that habituation rate was greater during the first two trial blocks.

Conclusions

In conclusion, the results of the present experiment can be summarized as follows. First we found habituation of both SCR and ERP responses to target stimuli in an "oddball" task. The habituation was rapid during the first 10-12 trials for both responses but decrements were evident across all 30 habituation trials. Interesting, while little or no differences were found in habituation of the SCR to target and nontarget stimuli, habituation of P300 amplitude was greater to the target stimulus. There was relatively little habituation of the P300 response to the nontarget. The differential habituation of SCR and ERP responses to target and nontarget stimuli may indicate fundamental differences in the characteristics of the underlying response systems. On the other hand, the ERP response may simply have been more sensitive to the experimental conditions. Further research is needed.

Second, we found evidence of dishabituation of the ERP response but not the SCR response. The latter was not expected. Again it may be either that OR and ERP response systems have different properties or that ERPs are more sensitive to the experimental conditions.

In conclusion, the present experiment suggests that including orienting response measures in ERP paradigms may be useful in providing information about the differences in the properties of ERP and OR response systems. It may be that the ERP is more sensitively related to the experimental conditions associated with orienting. Measures of central activity may provide the opportunity for a more direct analysis of the mechanisms producing the CR (Donchin et al., 1984).

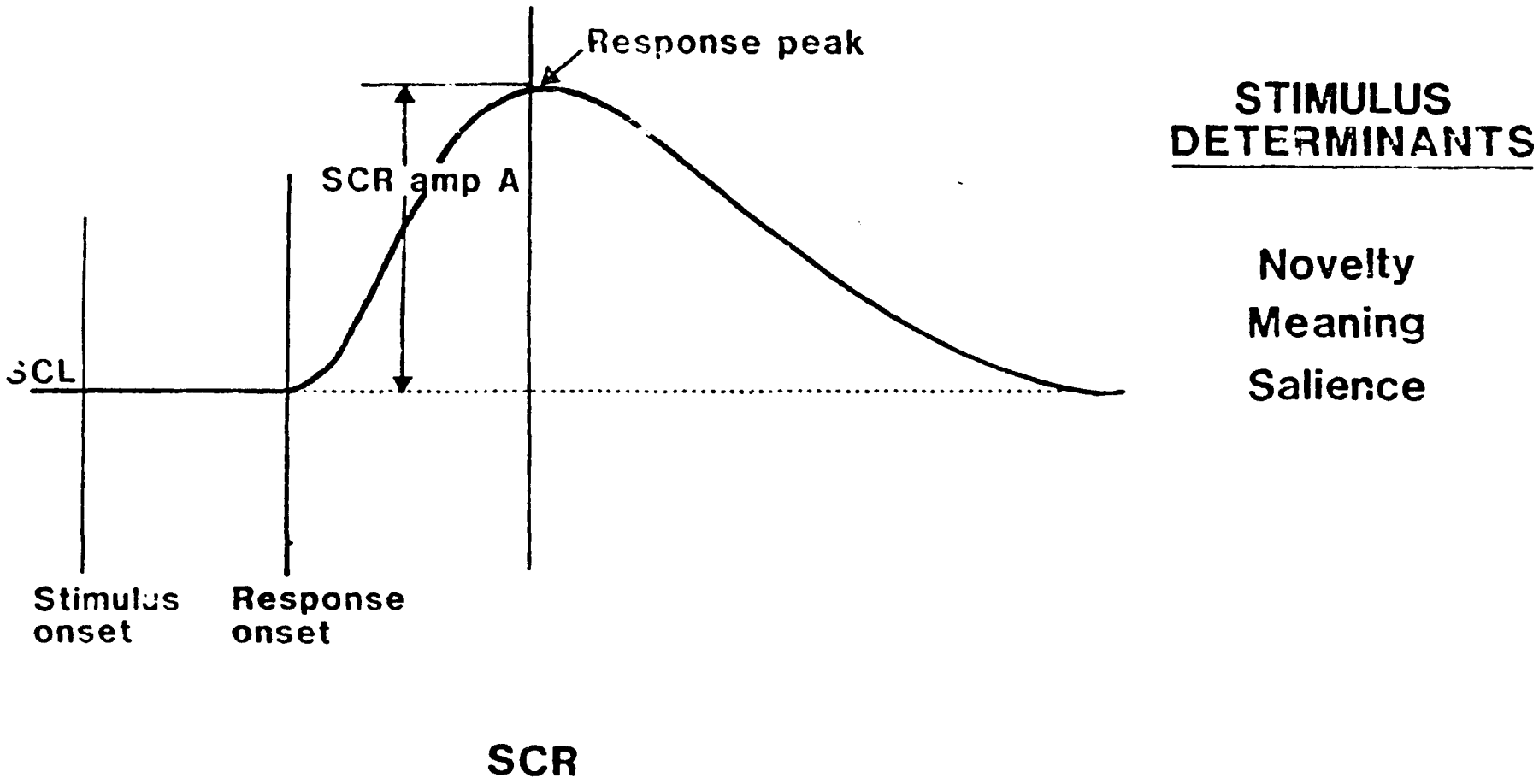
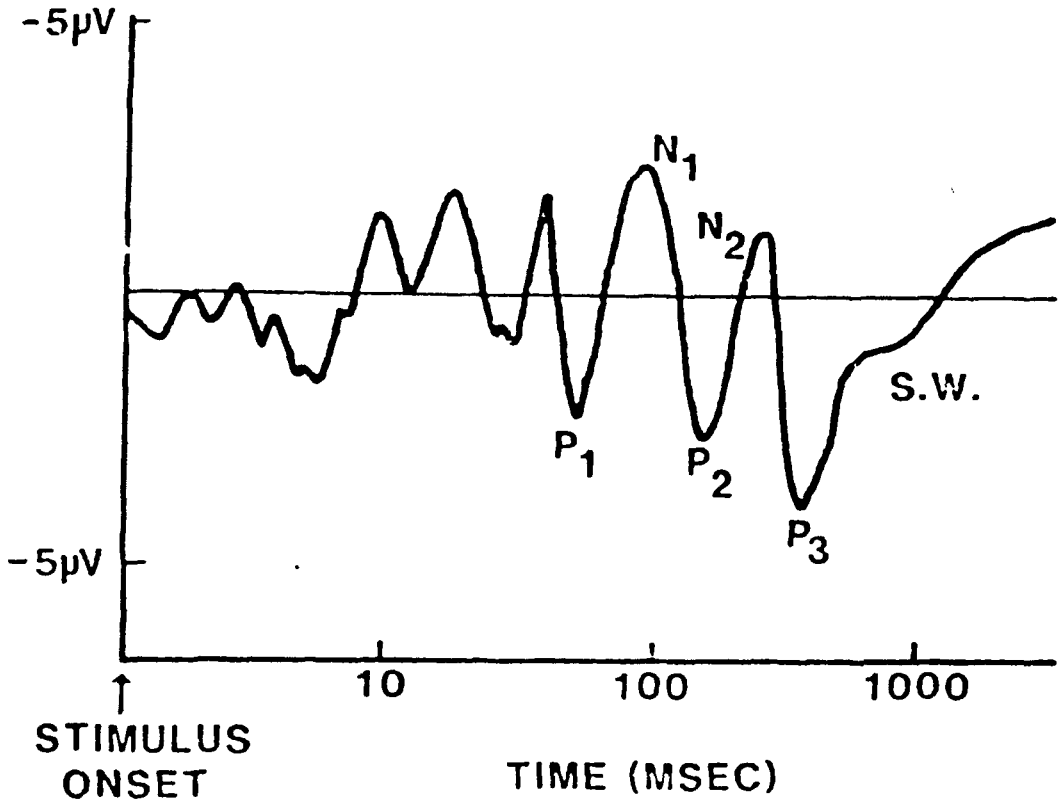


Figure 1 - Illustration of a skin conductance response



STIMULUS DETERMINANTS

Novelty

Meaning

Salience

ERPs

Figure 2 - Illustration of an event-related potential

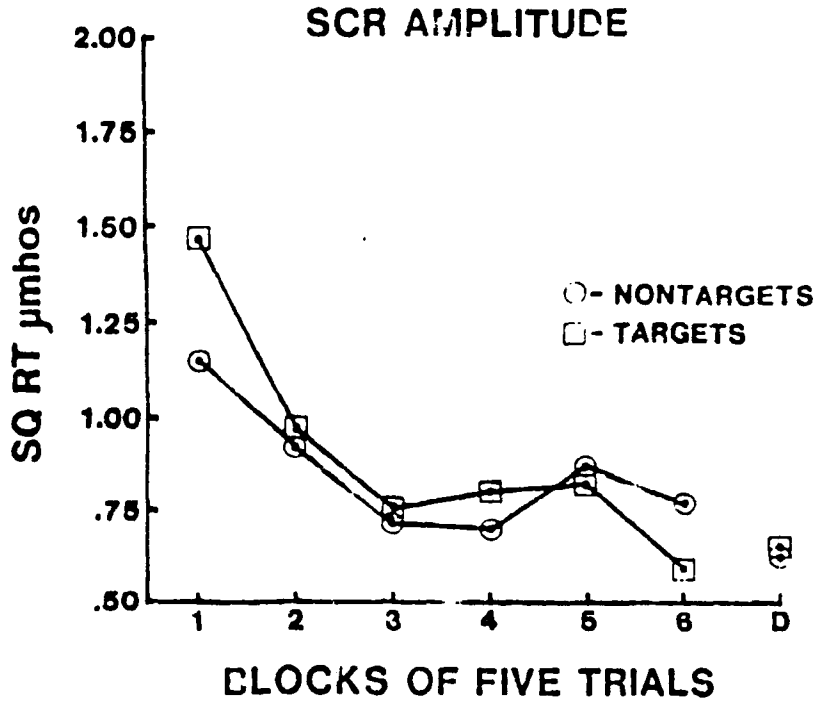


Figure 3 - SCR averaged for seven blocks of five trials

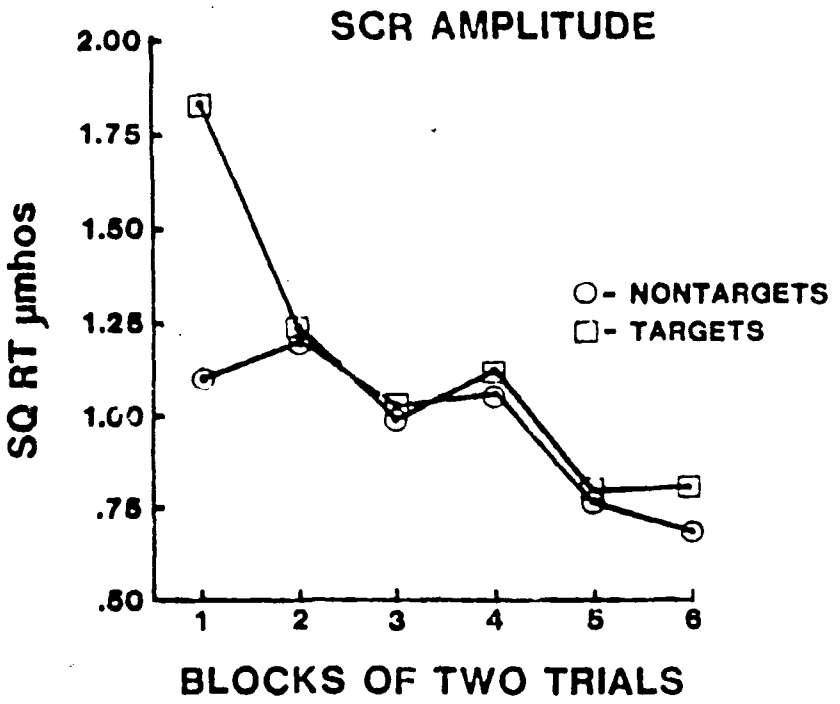


Figure 4 - SCR for six blocks of two trials

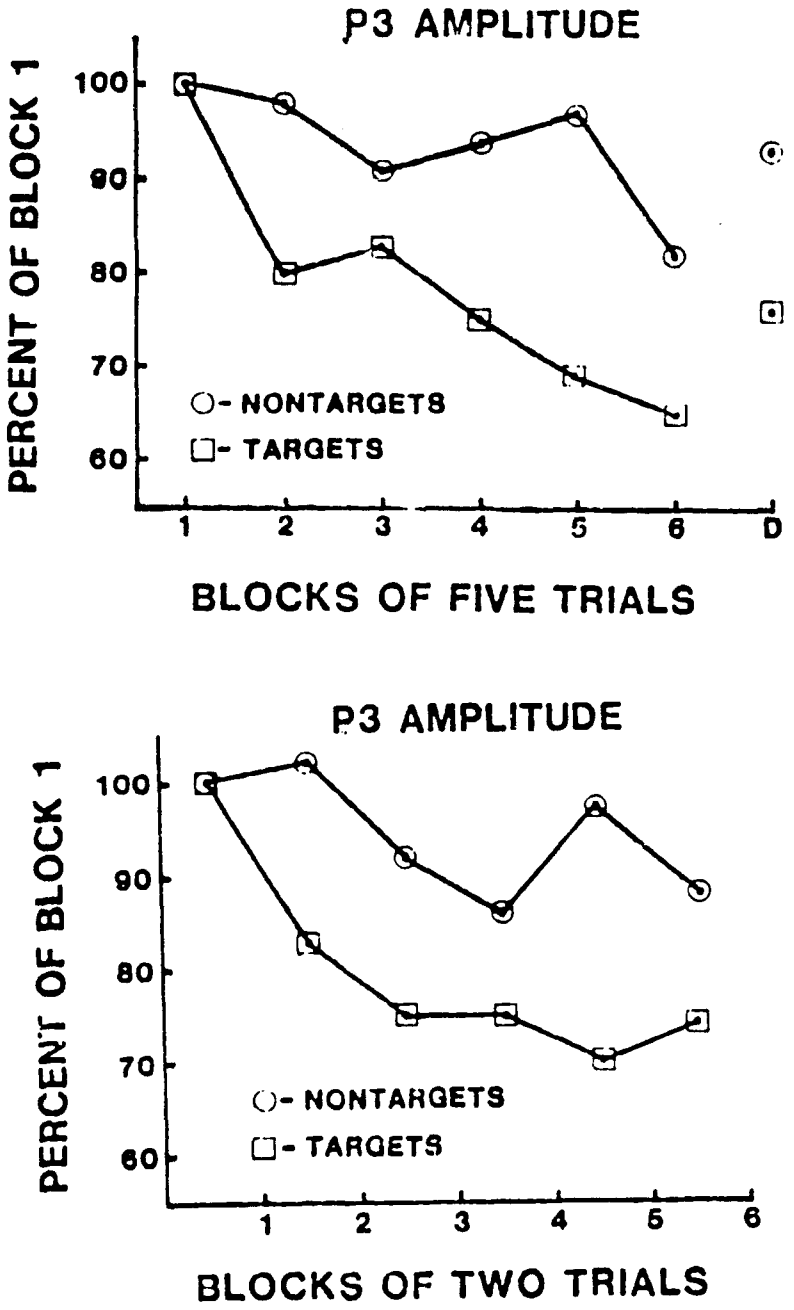


Figure 5 - P300 for seven blocks of five trials (top)
P300 for six blocks of two trials (bottom)

References for Experiment 2

Thompson, R. F., & Spencer, W. A. (1966). Habituation: A model phenomenon for the study of neuronal substrates of behavior. Psychological Review, 73, 16-43.

Donchin, E., Heffley, E., Hillyard, S.A., Loveless, N., Maltzman, I., Ohman, A., Rosler, F., Ruchkin, D., & Siddle, D. (1984). Cognition and event-related potentials II: The orienting reflex and P300. In Karrer, R., Cohen, J., & Teuting, P. (Eds.) Brain and Information: Event-Related Potentials. The New York Academy of Sciences, New York: New York.

6.3 Experiment 3 - Event-related Potentials Across Three Phases of Pavlovian Conditioning

Pavlovian conditioning has received much systematic investigation since the original work by Pavlov in the early 1900's. As research has continued, a broader role has been assigned to Pavlovian conditioning as it relates to everyday behavior (Rescorla, 1988; Turkhan, 1989). In addition, more cognitive explanations have been offered to explain the conditioning process. The goal of the present paper is to provide a conditioning paradigm in humans in which brain event-related potentials (ERPs) can be used as indices of learning.

Much early research on human Pavlovian conditioning consisted of measuring conditioned eyeblink responses (e.g., Spence, 1956). Psychologists have more recently focused on psychophysiological measures to index Pavlovian conditioning in humans. These measures include muscle activity, skin conductance, heart rate, vasomotor activity, and event-related potentials. With the exception of event-related potentials, a substantial literature exists relating the above measures to Pavlovian conditioning. However, ERPs possess several advantages when compared with peripheral measures. First, researchers are optimistic that ERPs provide a more direct index of information processing than the peripheral measures. That is, factors associated with physiological mechanisms in the periphery are not an issue with ERPs. Second, ERPs occur concurrently with stages of information processing and return quickly to baseline. In contrast, peripheral responses generally exhibit a longer onset latency and a longer return to baseline. These characteristics of peripheral response systems restrict the experimental tasks which can be studied.

One traditional advantage of peripheral measurement has been the ability to perform a trial-by-trial analysis of conditioning. However, recent statistical procedures now enable the same type of single-trial analysis with various ERP waves (Birch, Lawrence, & Hare, 1988; Chase, McCarthy, Squires, & Schanveldt, 1984; Fabiani, Gratton, Karis, & Donchin, 1987; Kenemans & Verbaten, 1988; Loveless, Simpson, & Naatanen, 1987; Pritchard, Brandt, & Barratt, 1986; Ruchkin & Glaser, 1976). The most common method of single trial ERP analysis involves digital filtering. This procedure reduces "noise" by filtering out those frequencies in the waveform that are not of interest.

As noted, the literature relating ERPs to Pavlovian conditioning is sparse. Of the ERPs, the CNV wave has received the most attention. Increases in CNV amplitude have been observed during eyeblink conditioning (Walter et al., 1964) and also during pairing of a tone with a phobic slide (Lumsden, Fenton, & Howard, 1980), a buzzer (Proulx & Picton, 1980), and a flash of light (Laffont, Bruneau, Jusseaume, & Lelord, 1977; Marineau, Garreau, Barthelemy, & Lelord, 1984). The CNV also increases when subjects learn that one stimulus predicts a second

stimulus which requires a speeded response (Low, Borda, Frost, & Kellaway, 1966) and when subjects learn paired associates (Peters, Billinger, & Knott, 1977). Furthermore, the CNV does not simply exhibit a linear increase in amplitude as one stimulus repeatedly predicts another stimulus. The above studies show an increase in the CNV during initial acquisition trials with a subsequent decrease thereafter. Findings relating the other ERPs to Pavlovian conditioning are few and mixed. For N100 amplitude, two studies report an increase as a result of conditioning (Begleiter & Platz, 1969; Syndulko et al., 1975) while several studies report no change (Hugdahl & Nordby, 1988; Marineau et al., 1984; Proulx & Picton, 1980). For P300, all but one study (Proulx & Picton, 1980) show an increase in amplitude during Pavlovian conditioning (Hugdahl & Nordby, 1988; Marineau et al., 1984; Peters et al., 1977; Raine & Venables, 1987; Syndulko et al., 1975). Only one study (Peters et al., 1977) examined changes in P300 across trials within the learning phase. In this study, P300 amplitude increased until the point where learning was complete and remained stable thereafter.

Few studies which assessed the relationship between Pavlovian conditioning and event-related potentials provided methodological details (several of the reports were abstracts). In addition, several studies used a methodology which rendered the findings ambiguous (Begleiter & Platz, 1969; Laffont et al., 1977; Marineau et al., 1984; Proulx & Picton, 1980). Finally, no study provided a detailed analysis of event-related potential changes across learning trials.

Although few studies have focused on brain measures of Pavlovian conditioning, the theoretical notions underlying several of these ERP components suggest that they are good candidates for indexing the learning process. For example, an increase in P300 amplitude has been related to increased stimulus significance, increased attentional resources to the stimulus and updating of memory. The CNV has been related to association, expectancy, attention and motivation. Many or all of the above processes would also seem to be involved when one stimulus becomes associated with (predictive of) another stimulus which is inherently significant, that is, during Pavlovian conditioning.

Research Hypotheses - Habituation Phase For the CNV to occur, a two-tone paradigm in which one stimulus predicts the occurrence of another stimulus is necessary. Therefore, since only single stimuli are presented during the habituation phase of testing, the CNV should be absent from all trials. The literature suggests that during the habituation phase the amplitude of N100 to both tones should be large initially and diminish rapidly to a stable amplitude (e.g., Ohman & Lader, 1977; Roth & Kopell, 1969). The P300 component should also occur initially but then decrease to near zero across the habituation phase (e.g., Courchesne, Courchesne, & Hillyard, 1978; Megela & Teyler, 1979).

Research Hypotheses - Acquisition Phase During acquisition, the CS+ becomes predictive of an aversive stimulus

(US) and the CS- becomes predictive of US absence. Based on previous research, CNV amplitude is predicted to increase during conditioning. Evidence also suggests that once the relationship is learned, the CNV will show a decrease in amplitude. These predictions fit the theoretical notion that the CNV reflects the cognitive resources involved in preparing to evaluate a stimulus. During learning, the subject will focus on whether the US follows each stimulus presentation. Therefore, a CNV may be observed initially to both CS+ and CS-. Further learning may result in an increase in CNV amplitude to CS+ and a decrease to CS-. However, if US absence following the CS- is interpreted by the subject as an event of "safety" then a CNV to CS- may also increase with further learning. Once learning is complete any CNV which has developed should decrease since no further evaluation of the presence or absence of the US is required.

Empirical findings and theoretical notions related to the N100 wave during acquisition are few and mixed. If N100 reflects attention to the auditory channel, one would expect a large N100 to both CS+ and CS- as long as aversive auditory events continue to be presented. That is, there should be an increase in N100 amplitude from the end of the habituation phase to the beginning of the acquisition phase.

The literature suggests that during the acquisition phase, the P300 to the CS+ should increase in amplitude as the subject learns the predictive relationship. The pattern of P300 amplitude once learning is complete is less clear. From a theoretical perspective, acquisition should involve memory associations being formed and the subject learning that the CS+ is a meaningful event. Both updating of memory and increased meaningfulness should result in an increase in P300 amplitude. Furthermore, the same rationale may apply to the CS-. That is, the CS- becomes predictive of a period of "comfort" (US absence). Learning this association may give meaningfulness to the CS-, thus resulting in an increased P300.

Research Hypotheses - Extinction Phase During the extinction phase the US is no longer presented. While CNV amplitude is expected to decrease toward the end of the acquisition phase, terminating US presentation will require the subject to reallocate resources to the events occurring at tone termination. Therefore, CNV amplitude to both tones may increase at the beginning of the extinction phase. As the extinction phase progresses, CNV amplitude should decrease. In addition, absence of the aversive auditory event should result in a decrease in attention to auditory input, and therefore, a decrease in N100 amplitude. Likewise, the meaningfulness of both CS+ and CS- should diminish, with a resulting decrease in P300 amplitude to both tones. Although both CS+ and CS- now predict "comfort", in relative terms comfort is not important since there are no longer periods of aversiveness.

Methods

Subjects Thirty undergraduate students (eighteen males, twelve females) served as subjects (ages 18-24). Subjects

received one hour of experimental credit for their participation.

Apparatus Event-related potentials and eye movements/blinks were recorded using Beckman silver-silver chloride electrodes. The EEG signals were amplified and filtered by Grass 7P122 D.C. amplifiers. For EEG signals, the time constant was 5.0 s and the high frequency filter was set to 35 Hz. The EOG (eye movements/blinks) was amplified by a Grass 7P1 D.C. Preamplifier (time constant = 5.0 s) and 7DA Driver Amplifier (high frequency filter = 35 Hz). The EEG and EOG were digitized at 200 Hz beginning 0.2 s prior to tone onset and continuing until 2.0 s after tone onset.

Procedure

Electrodes were affixed to the subject's scalp at Fz, Cz, Pz, A1, and A2 sites according to the 10-20 international system. Additional electrodes were placed above and below the right eye to record eye movements and blinks. An earclip electrode served as ground. Electrode impedance was kept below 5.0 Kohm for EEG sites and below 10.0 Kohm for EOG. Subjects were instructed that tones and loud noises would be presented. During the session, they were to simply listen to the stimulus presentations. They were also instructed to fixate their eyes on a small dot on the opposite wall.

Habituation phase Two tones (to be CS+ and CS-) of 1000 Hz and 2000 Hz were presented. Tone intensity was 75 dB and tone duration was 1.0 s. During this phase of testing, each tone was presented fifteen times. Order of tones was random (ISI=3-5 s).

Conditioning phase The conditioning phase followed the habituation phase without interruption (i.e., there was a 3-5 s interval). During this phase, one of the two tones (1000 Hz or 2000 Hz) was designated CS+ (to be paired with the US) and the other tone was designated CS-. The designation was counterbalanced across subjects. The interval between tones continued to be 3.0 to 5.0 s and each tone was presented fifteen times. Following each presentation of CS+, the US (white noise, 100 dB, 1.0 s) was presented. The US occurred concurrent with CS+ termination.

Extinction phase The extinction phase followed the conditioning phase without interruption. The parameters were identical to those of the habituation phase; each tone was presented fifteen times. The US was not presented during the extinction phase.

Immediately following the extinction phase, the subject completed a questionnaire which assessed the point at which they learned the CS+/US relationship.

ERP scoring Contribution of eye activity to scalp recordings was removed on each trial using a procedure described by Gratton, Coles, & Donchin (1983). After eye artifact was removed, waveforms were digitally filtered and CNV, N100 and P300 amplitude scored.

In order to facilitate the scoring of ERPs on a single trial basis, waveforms were digitally filtered (BMDP1T) to eliminate

frequencies outside the range of interest. Two different filtering procedures were used to improve the signal-to-noise ratio. The first procedure facilitated scoring of the CNV. With the stimulus parameters used in the present study, the CNV is a slow negative wave which begins from 260-460 ms after tone onset and increases in amplitude until occurrence of the second stimulus 1000 ms after tone onset (Tecce, 1972). This pattern of amplitude change implies that much of the power of the CNV consists of frequencies below 1.0 Hz. Therefore, a filter was used which allowed the slower frequencies (below 2.0 Hz) to pass but attenuated higher frequencies. The CNV was scored as the mean amplitude of the waveform from 900-1000 ms post-tone onset (100 ms prior to US onset) minus the amplitude of the 200 ms baseline prior to tone onset.

The second filtering procedure was designed to facilitate scoring of N100 and P300 peaks. The power of these latter waves resides in frequencies of 3.0 Hz (P300) to 6.0 Hz (00) (Pritchard, Brandt, & Barratt, 1986; Ruchkin & Glaser, 1976). Therefore, the second filter (which actually consisted of two filters) attenuated frequencies above and below the 3.0 to 6.0 Hz range. Amplitude scores for the waveform peaks were defined as the maximal peak within a specified latency range minus the mean amplitude of the baseline. The latency ranges following onset of CS+ and CS- were 80-150 ms for N100 and 290-450 ms for P300. These latency ranges were determined by inspecting the average waveforms. If no peak was found within a given latency range, the amplitude and latency values were interpolated based on the scores of the two trials preceding and two trials subsequent to the missing trial.

Results

Amplitude scores were recorded for each tone presentation across each phase of the study (total presentations = 45 CS+, 45 CS-). Examination of the data revealed substantial changes in component amplitude and latency from one trial to the next trial within a test phase, i.e., considerable variation from trial to trial. Therefore, the scores were averaged across every three trials to create five blocks of three trials for each phase of the study.

The post-session questionnaire revealed that eleven of the thirty subjects could not report the relationship between the CS+ and the US during the acquisition phase. Therefore, a Group factor (learners, non-learners) was added to the analyses.

Initial analyses revealed that the scalp site interacted rarely with the other factors. Therefore, since amplitudes were generally largest at the Cz site, analyses reported below utilized scores from the Cz site only and incorporated the Group (learners, non-learners) factor. Thus, for each phase of testing, a three-way mixed ANOVA was performed, with the between factor being Group (learners, non-learners) and the within factors being Tone type (CS+, CS-) and Block (Blocks 1-5). (Note: Greenhouse-Geisser degrees of freedom adjustment was used for repeated measures analyses and corresponding p values

reported.)

While most predictions in the present study related to ERP changes across a particular phase of testing, several predictions related to changes occurring from the end of one phase to the beginning of the next phase. To test the latter predictions, a three-way mixed ANOVA was performed, with the between factor being Group (learners, non-learners) and the within factors being Tone type (CS+, CS-) and Block (Block 5 to Block 1).

Habituation Phase - CNV wave While it was predicted that no CNV would be observed during the habituation phase (since no second stimulus followed the tones), results showed that a small CNV was present. The pattern of CNV amplitude for learners and non-learners across phases is illustrated in Figure 1. For both groups, a small CNV was present on Block 1 for both tones. The CNV then asymptoted to a level near 2.0 uV across Blocks 2-5. The three-way ANOVA (Group X Tone type X Block) revealed no significant effects for CNV amplitude across the habituation phase.

N100 peak. Figure 2 shows the amplitude of N100 across the three test phases for learners and nonlearners. Focusing first on the N100 peak for learners, it can be seen that N100 amplitude to both tones decreased as predicted from 14.7 uV to 11.5 uV across the habituation phase. Furthermore, it appeared that by the end of the habituation phase N100 amplitude still did not reach an asymptotic level. The pattern of N100 change appeared more variable for the non-learners. Although there appeared to be a decrease for learners, the three-way analysis revealed no significant effects for N100 amplitude across the habituation phase.

P300 peak. As predicted, P300 to both tones decreased rapidly to an asymptotic level across the habituation phase (see Figure 3). The pattern of change was similar for both learners and non-learners. Across conditions, P300 amplitude decreased from 9.7 uV on Block 1 to 7.0 uV on Block 2. The amplitude stabilized near 7.0 uV across Blocks 2-5. The three-way analysis showed only a main effect for Block ($F(4,112)=5.42$, $p.<.01$), which indicated that the initial decrease in both groups was significant.

Acquisition Phase - CNV wave. For learners and non-learners the CNV to both tones showed a marked increase in amplitude across the acquisition phase (see Figure 1). This increase continued through the end of the 15 acquisition trials with no indication that the CNV measure had asymptoted. Furthermore, there appeared to be some differences between the CS+ tone and the CS- tone and for learners and non-learners. The increase in CNV for both groups appeared more marked for the CS+ than for the CS-. The CNV to the CS+ increased from about 2.0 uV to about 13.0 uV across the acquisition phase, while the CNV to CS- only increased from about 4.0 uV to about 8.5 uV. It can also be seen in Figure 1 that the nature of the CNV increase in learners appeared different from that of non-learners. For learners, the CNV increased markedly across Blocks 1-3, with the CNV to CS+

becoming larger than the CNV to CS- on Block 2. For non-learners, the CNV did not show a marked increase until Blocks 3-5, and the CNV to CS+ did not become larger than the CNV to CS- until Block 4. The reliability of the above observations was assessed with a three-way ANOVA (Group X Tone type X Block). The analysis confirmed that the main effect for Block was significant ($F(4,112)=5.23$, $p.<.01$), but that the interactions of Tone type X Block and Group X Block described above did not reach significance. As noted above, CNV changes were still occurring at the end of the acquisition phase. The differential effect for CS+ and CS- (Tone type X Block interaction) may have been more apparent if additional acquisition trials had been given.

N100 peak. It was predicted that the amplitude of N100 to both tones would increase from the end of the habituation phase to the beginning of the acquisition phase. Figure 2 shows that this increase was apparent for learners but not for non-learners. For learners, the amplitude of N100 to both CS+ and CS- increased 2.5 uV from Block 5 of the habituation phase to Block 1 of the acquisition phase. For non-learners, there was no systematic change across this same period. A three-way ANOVA (Group X Tone type X Block) assessed changes from Block 5 of habituation to Block 1 of acquisition. This analysis showed no significant effects, including the Group X Block interaction described above ($p=.09$). However, the considerable variability in the non-learners group may have masked the differences in the learners group. Therefore, to eliminate variability due to non-learners and to focus on N100 changes for the learners, a two-way within ANOVA (Tone type X Block) was performed for the learners group only. This analysis did show a main effect for Block ($F(1,18)=4.76$, $p.<.05$), thus providing evidence for the increase in N100 amplitude from the end of habituation to the beginning of acquisition (for learners).

The amplitude of N100 across the acquisition phase showed unexpected but interesting results. For both learners and non-learners, amplitude of N100 to CS+ was generally larger than to CS- across the acquisition phase. From the figures it appeared that N100 amplitudes to both CS+ and CS- were similar on Block 1. Following Block 1, N100 amplitude to CS+ increased to a maximum value of 16.7 uV on Block 3 (non-learners) or Block 4 (learners) and showed a slight decrease across the remaining trials. The three-way analysis revealed only a main effect for Tone type, $F(1,28)=6.09$, $p.<.05$. The Tone type X Block interaction was not significant.

P300 peak. Contrary to expectations, the amplitude of P300 to CS+ did not show an increase across the acquisition phase. Figure 3 suggests that, for learners only, the amplitude of P300 to CS- showed an increase across the acquisition phase. For learners, the P300 to CS+ decreased from Block 1 (5.5 uV) to Block 4 (3.5 uV), with an increase from Block 4 to Block 5 (5.0 uV). Further, it appeared that the amplitude of P300 to CS- was still increasing at the end of the acquisition phase. In contrast to the P300 effects observed for learners, Figure 3

shows that, for non-learners, the amplitude of P300 to both the CS+ and the CS- across the acquisition phase was variable, with a general decrease in amplitude of 2.0 uV for both tones.

While the above observations suggested that learners showed an increase in amplitude of the P300 to CS-, the three-way interaction (Group X Tone type X Block) was not significant. In addition, no other effects were significant. Although the three-way interaction did not reach significance, the trial-to-trial variability in the non-learner group may have masked the CS+/CS- differences in the learner group. To eliminate the variance contributed by non-learners and to focus on changes in P300 amplitude for learners, a two-way within ANOVA (Tone type X Block) was performed for the learners group only. The two-way analysis did show a main effect for Tone type, $F(1,18)=4.83$, $p.<.05$, but did not reveal a Tone type X Block interaction. Thus there was some statistical evidence for a larger P300 to CS- than to CS+ in the learners group. As noted above, P300 amplitude was still changing at the end of the acquisition phase. Therefore, additional acquisition trials may clarify these interesting differences.

Extinction Phase - CNV wave. During the acquisition phase (see above), the CNV increased across blocks. As expected, during the extinction phase the CNV decreased from Block 1 to Block 5 (see Figure 1). Like the acquisition phase, the effect appeared delayed in the non-learner group. The three-way ANOVA confirmed these observations. There was a main effect for Block, $F(4,112)=4.15$, $p.<.01$, and a Group X Block interaction, $F(4,112)=3.27$, $p.<.05$.

N100 peak. As described above, the acquisition phase resulted in a larger N100 to CS+ than to CS-. However, the extinction phase resulted in similar amplitudes for both CS+ and CS-, with amplitude to both tones showing an overall expected decrease across extinction blocks. Although an overall decrease was observed for both learners and non-learners, learners appeared to show an initial increase in N100 amplitude from Block 1 to Block 2 of the extinction phase which was not apparent for non-learners. The overall decrease was reflected by a main effect for Block, $F(4,108)=3.84$, $p.<.01$. No other effects were significant.

P300 peak. It can be seen in Figure 3 that P300 amplitude, in general, increased from Block 5 of the acquisition phase to Block 1 of the extinction phase. The three-way ANOVA (Group X Tone type X Block) which assessed these changes from Block 5 to Block 1 showed a main effect for Block, $F(1,28)=5.05$, $p.<.05$. No other significant effects from the end of acquisition to the beginning of extinction were observed.

Following this initial increase in P300 amplitude at the beginning of the extinction phase, there appeared to be a small (2.0 uV) decrease in the amplitude of P300 to CS+ across the extinction phase. The amplitude of P300 to CS- changed little across these same periods. The three-way analysis which assessed changes across the extinction phase showed no significant effects

for P300 amplitude.

Discussion

A summary of the results across the habituation, acquisition, and extinction phases of testing reveals several systematic changes. The habituation phase was designed to obtain stable ERP responding prior to beginning the acquisition phase. With the possible exception of N100 amplitude, the habituation phase served its purpose. During the acquisition phase, the CNV, N100, and P300 peaks appeared to index aspects of conditioning. For the CNV, amplitude to CS+ and CS- increased across the acquisition phase. Furthermore, the CNV increase appeared more marked for CS+ than CS-, and the CNV increase seemed to occur later for non-learners. For N100, the amplitude to CS+ was larger than to CS- for both learners and non-learners. For P300, there was some evidence in the learners group that P300 amplitude was larger to CS- than to CS+ across the acquisition phase. During the extinction phase the amplitude of CNV and N100 decreased. Like acquisition, the CNV decrease occurred later in the extinction phase for the non-learners.

Habituation Phase

The focus of the present study was on ERP changes as one learns predictive relationships during the acquisition phase. However, the habituation phase serves an important role. The habituation phase is designed to provide a stable baseline of ERP amplitude prior to presenting acquisition trials. There is a substantial literature which shows that initial presentations of novel stimuli (tones) result in relatively large orienting responses. When the stimuli are irrelevant (i.e., no task required), the orienting response decreases to a stable level within a few trials. In the present study, this stable level was generally achieved.

CNV wave. It was hypothesized that the CNV would be absent during the habituation phase since a second stimulus never followed the tones. However, there appeared to be a negative component on Block 1 (6.0 uV), with a slight negativity persisting across Blocks 2-5 (2.0 uV). This wave may be the "sustained potential" described by Picton, Woods, and Proulx (1978) which occurs in response to the continuation of a stimulus. Naatanen and Picton (1987) have also described a "processing negativity" which is observed as long as an attended stimulus is processed.

N100 peak. A number of studies demonstrate habituation of N100 amplitude to "nontarget" tones (e.g. Ohman & Lader, 1977; Roth & Kopell, 1969; Woods & Elmasian, 1986). The present results showed a trend in this direction. Failure to fully replicate these findings and to confirm predictions may relate to two factors. First, instructions to subjects to " ... listen carefully to the sounds that you hear" may have given the tones some "target" value. In addition, additional habituation trials would have likely resulted in a statistically significant decrement in N100 amplitude.

P300 peak. As hypothesized, P300 amplitude decreased across

the habituation phase. This finding is consistent with many other studies showing rapid habituation of the P300 to irrelevant stimuli (Courchesne, Courchesne, & Hillyard, 1978; Fruhstorfer, 1971; Lutzenberger, Schandry, & Birbaumer, 1979; Megela & Teyler, 1979; Picton & Hillyard, 1974; Squires et al., 1973). However, in the present study P300 amplitude did not approach zero. Rather, P300 amplitude stabilized with an amplitude of 7 uV over the last three blocks of the habituation phase. Like the interpretation of the N100 peak, this latter effect may have resulted from the instructions given to the subjects. Also, the mean interstimulus interval between presentations of the same tone was ten seconds. This is longer than most studies which assessed P300 habituation to irrelevant stimuli.

Acquisition Phase

The acquisition phase was the primary focus of the present study. Interest was in changes in central ERP measures as a result of making one of two tones predictive of an aversive event. From a traditional perspective, strict evidence for conditioning requires a change in response to the CS+ stimulus which is not observed for the CS- stimulus. However, more recent views of conditioning stress the relationships established between all events in the environment, not simply the relationship between the CS+ and the US. In the following sections, the results of the acquisition and extinction phases are evaluated in light of both traditional definitions of conditioning and more recent emphasis on the cognitive constructs involved in the subject's interpretation of the stimuli.

CNV wave. In the present study, the CNV to both CS+ and CS- increased markedly across the acquisition phase. While an initial increase in CNV to both tones was predicted, it was further hypothesized that the CNV to CS+ would increase until learning was complete and then the CNV to CS+ would decrease. However, the fact that one-third of the subjects could not report the CS+/US relationship suggests that additional acquisition trials may be required for complete learning.

After the initial CNV to CS-, it was predicted that the CNV to CS- may also increase (and subsequently decrease) if the absence of the US became an event of "comfort". Of the studies which examined the CNV component during conditioning, no study reported whether there was a CNV to the CS- stimulus. In fact, a number of the studies did not incorporate a CS- into the paradigm (Laffont et al., 1977; Marineau et al., 1984; Walter et al., 1964). Traditional views of Pavlovian conditioning emphasize the absence of a response to the CS- stimulus. However, in order to learn a predictive relationship one must learn a discrimination. That is, not only must an individual focus on the event following the CS+, the individual must prepare to evaluate the absence of that event following the CS-. The appearance of the CNV component following the CS- may reflect this latter preparation.

In addition to the above effects, the increase in CNV amplitude to both tones appeared delayed for non-learners relative to learners. This is particularly interesting since

non-learners exhibited a marked increase in CNV amplitude to CS+ across the last acquisition block. This increase resulted in a CNV amplitude to CS+ on Block 5 that was actually larger than the CNV on Block 5 for learners. In fact, several of the subjects classified as "non-learners" made statements like "It seemed that the noise followed one of the tones more often than the other, but I'm not sure". These findings suggest that changes in the CNV may predict awareness of relationships in the environment.

N100 peak. The amplitude of N100 proved to be a measure which indexed a discrimination between CS+ and CS- during the acquisition phase for both learners and non-learners. Two general factors which affect N100 amplitude include arousal level and attention to stimulation (Naatanen & Picton, 1987). Therefore, it was predicted that the aversive events occurring during the acquisition phase would increase both of these factors, and that N100 to both CS+ and CS- would be increased during the acquisition phase relative to the habituation phase. The results supported this prediction for learners, but also revealed a differential increase in amplitude to the CS+ relative to the CS- for both learners and non-learners.

Although several studies suggest an increased N100 when a particular channel of stimulus input is attended (e.g., Hillyard, Hink, Schwent, & Picton, 1973; Schwent & Hillyard, 1975), little research has focused on the effects when a particular stimulus within a channel of input is attended. The present results suggest that N100 amplitude may index attention to a particular stimulus and may be a central measure of Pavlovian conditioning. That is, Pavlovian conditioning may result in increased attention to the CS+ stimulus relative to the CS- stimulus.

It is interesting that the above findings and discussion for N100 apply to both learners and non-learners. In fact, the maximum amplitude to the CS+ tone during acquisition was slightly larger for non-learners and occurred one block earlier for them. One can speculate that these findings reflect some form of conditioning (learning) to which the subject remains verbally unaware. This type of learning may relate to why so many phobic individuals cannot verbalize the event(s) which resulted in their fearful associations.

P300 peak. In addition to N100 amplitude showing a discrimination between CS+ and CS- during acquisition, there was some evidence that P300 amplitude also showed this discrimination. Furthermore, this discrimination was only observed for learners. However, the pattern of P300 change for learners was contradictory to what was hypothesized. There appeared to be an initial suppression of P300 amplitude to both the CS+ and CS- at the beginning of the acquisition phase. While P300 amplitude to the CS- recovered to a baseline of 7.0 to 8.0 uV (level at the end of the habituation phase), P300 amplitude to CS+ remained small (4.0 to 5.0 uV) throughout the acquisition phase. These results are difficult to interpret since no current theory of the P300 can incorporate these findings. Learning that CS+ predicted the US and that CS- predicted the absence of the US

was expected to make both tones more "meaningful". In addition, the memory updating process involved in this learning was expected to increase P300 amplitude, especially to the CS+. Furthermore, the present results with P300 are contradictory to one previous report of a larger P300 to the CS+ than the CS- during acquisition (Hugdahl & Nordby, 1988). One can speculate regarding this unexpected outcome.

The present study may be different from other studies which examined factors affecting P300 amplitude. The aversive stimuli presented during the acquisition phase may have resulted in a state of fear or extreme arousal due to the aversive event (intense noise). While both the present study and other studies (e.g., Roth, Blowers, Doyle, & Kopell, 1982) have recorded large P300s to intense auditory stimuli, P300s in the presence of stimuli predicting aversive events have not been examined. Perhaps the stage of information processing indexed by the P300 is adversely affected under these conditions. In support of this notion, there is a body of evidence suggesting that performance on some tasks is impaired under high levels of emotional arousal (e.g., Easterbrook, 1959; McKenna, 1986; Morris, Davis, & Hutchings, 1981; Sarason, 1980; Wine, 1980).

The above interpretation must be explained in relation to the findings of Hugdahl and Nordby (1988). These researchers found a larger P300 to CS+ than to CS- as a result of eight acquisition trials. The stimuli used by Hugdahl and Nordby (1988) were similar to those in the present study. However, in their study the mean time interval between presentations of the white noise was eighty seconds, whereas the mean interval in the present study was eight seconds. Therefore, the level of arousal at the onset of each tone may have been much lower in their study. While this interpretation may be incorrect, other interpretations of the P300 findings are difficult to formulate. It is clear that current theoretical interpretations of the P300 must be modified to explain the current findings.

Extinction Phase The extinction phase is used in Pavlovian conditioning studies to observe a reduction in conditioned responding once the unconditioned stimulus is removed from the environment. In the present study, this reduction was observed for both CNV and N100 amplitude.

CNV wave. A decrease in CNV amplitude to both the CS+ and the CS- was observed across extinction trials, with the decrease occurring later for the non-learners. It was predicted that the CNV would decrease across extinction trials as the subject learned that no second stimulus followed tone presentation. This finding supports the notion that the CNV reflects the cognitive resources involved in preparing to evaluate an upcoming stimulus event. As the subject learned that a second stimulus was no longer presented, there was no need for cognitive preparation. The difference observed between learners and non-learners during the extinction phase fit well with the differences observed during the acquisition phase. During acquisition, the CNV results suggested that it took longer for non-learners to begin

to learn the CS+/US association. Likewise, during extinction, the CNV results suggest that it took longer for non-learners to realize that no further aversive stimuli would be presented.

N100 peak. It was hypothesized that elimination of the aversive stimulus would lead to a decrease in attention to the tones, as indexed by N100 amplitude. This prediction was confirmed. While there was an overall decrease in N100 amplitude across the extinction phase, learners appeared to show an initial increase in N100 amplitude from Block 1 to Block 2 before showing a subsequent decrease. Non-learners did not exhibit this initial increase. One can speculate that once learners realized that the sequence of stimulus events had changed, learners reoriented to the tones in order to reevaluate the stimulus environment. Non-learners may not have made this effort.

P300 peak. No significant change in the P300 component was observed across extinction trials, although learners showed a slight decrease. While a decrease in amplitude was predicted, the prediction was based on the assumption that "meaningfulness" and memory updating would be relevant factors during the acquisition phase. As discussed above, this assumption was contradicted by the findings during the acquisition phase. However, one aspect of the extinction phase is interesting and may support the "fear/arousal" interpretation provided for the P300 acquisition data. While P300 amplitude to CS- became larger across acquisition trials than P300 amplitude to CS+ (learners only), this difference was no longer apparent at the beginning of the extinction phase (and throughout the extinction phase). That is, from the end of the acquisition phase to the beginning of the extinction phase, the amplitude of P300 to CS+ recovered to baseline levels. Therefore, the association of the CS+ with fear/arousal may have extinguished rapidly once presentation of the US was terminated.

Summary

The present study showed that a discriminative Pavlovian conditioning paradigm resulted in systematic changes in the CNV, N100, and P300 event-related potential measures. During the acquisition phase of testing, CNV amplitude increased to both the CS+ and CS- tones. This may reflect the subject's preparation to evaluate both the presence of the US following CS+ and the absence of the US following CS-. In addition, the above effects seemed to occur later in the acquisition phase for subjects who could not report the CS+/US association (non-learners). Discriminative responding during the acquisition phase was evidenced by a larger N100 to CS+ than to CS- (for both learners and non-learners) and a smaller P300 to CS+ than to CS- (for learners only). The N100 results may reflect increased attention to the CS+ stimulus relative to the CS- stimulus during the acquisition phase. The P300 results may reflect an association with extreme arousal which impairs the processing indexed by the P300. Both CNV amplitude and N100 amplitude showed extinction across the final phase of testing. Overall, the results suggest that the use of central measures in addition to peripheral

measures, may provide a more complete understanding of the learning process underlying Pavlovian conditioning.

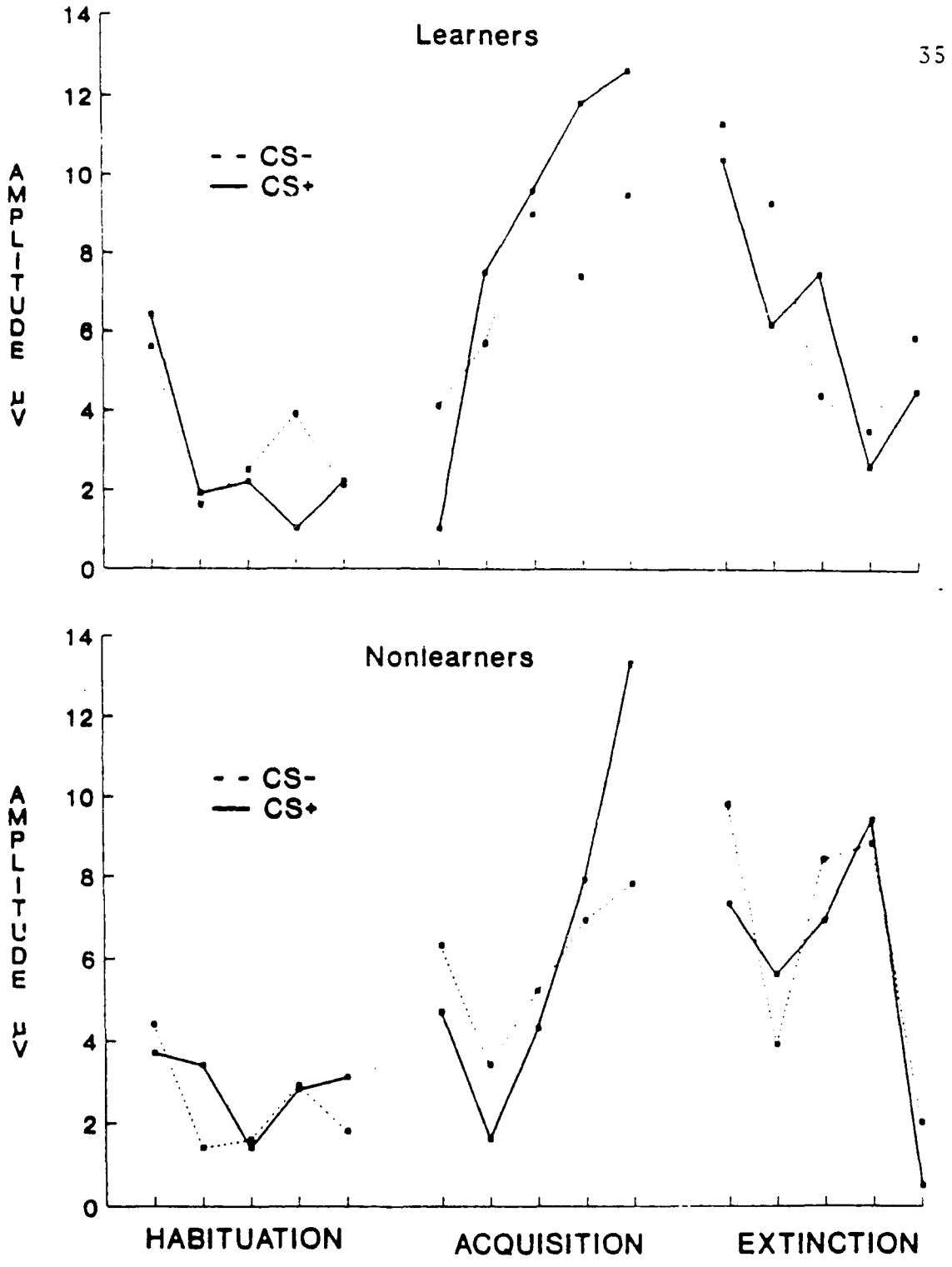


Figure 1 - CNV amplitude for learners and nonlearners across the three test phases

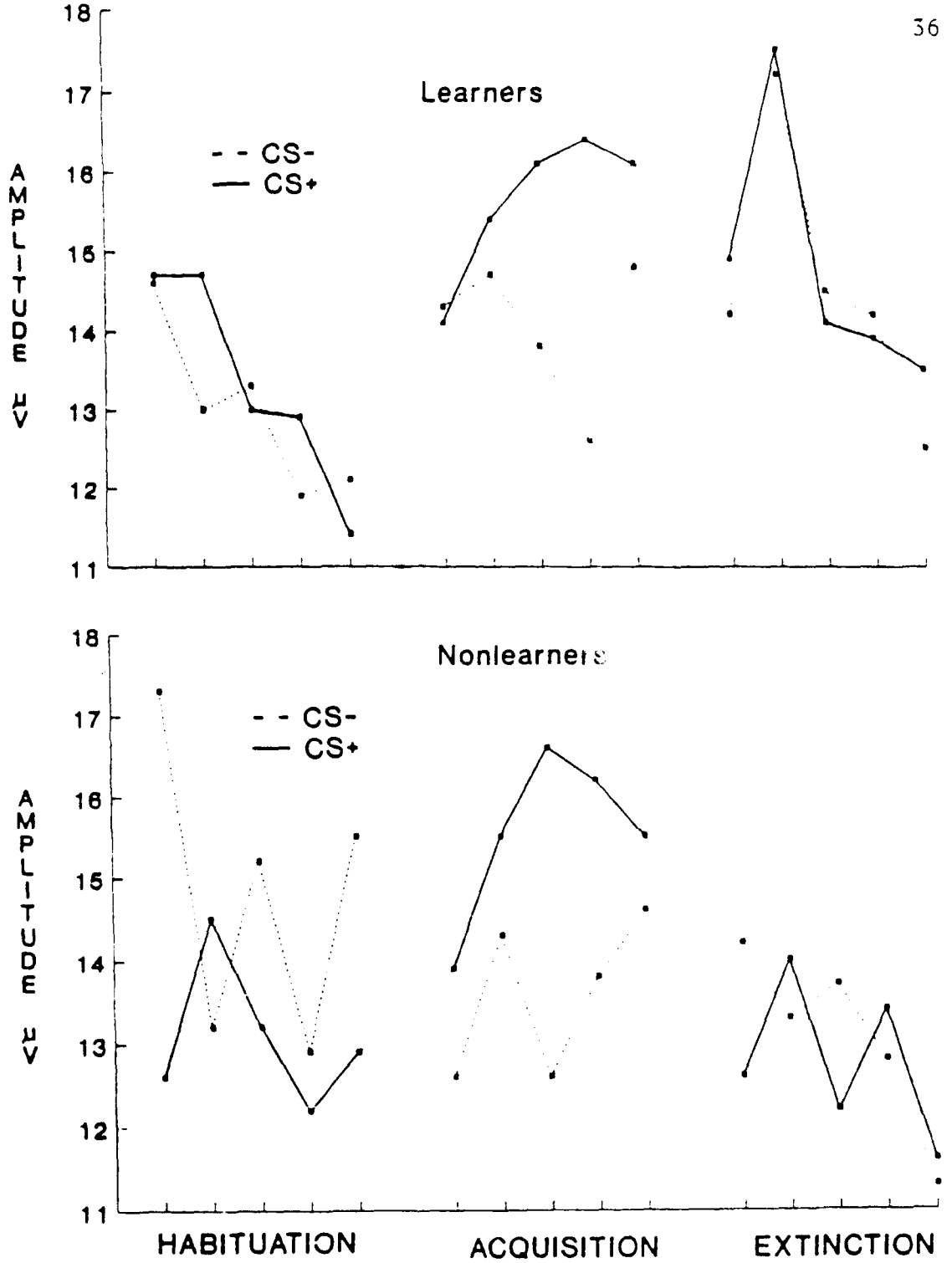


Figure 2 - N100 amplitude for learners and nonlearners across the three test phases

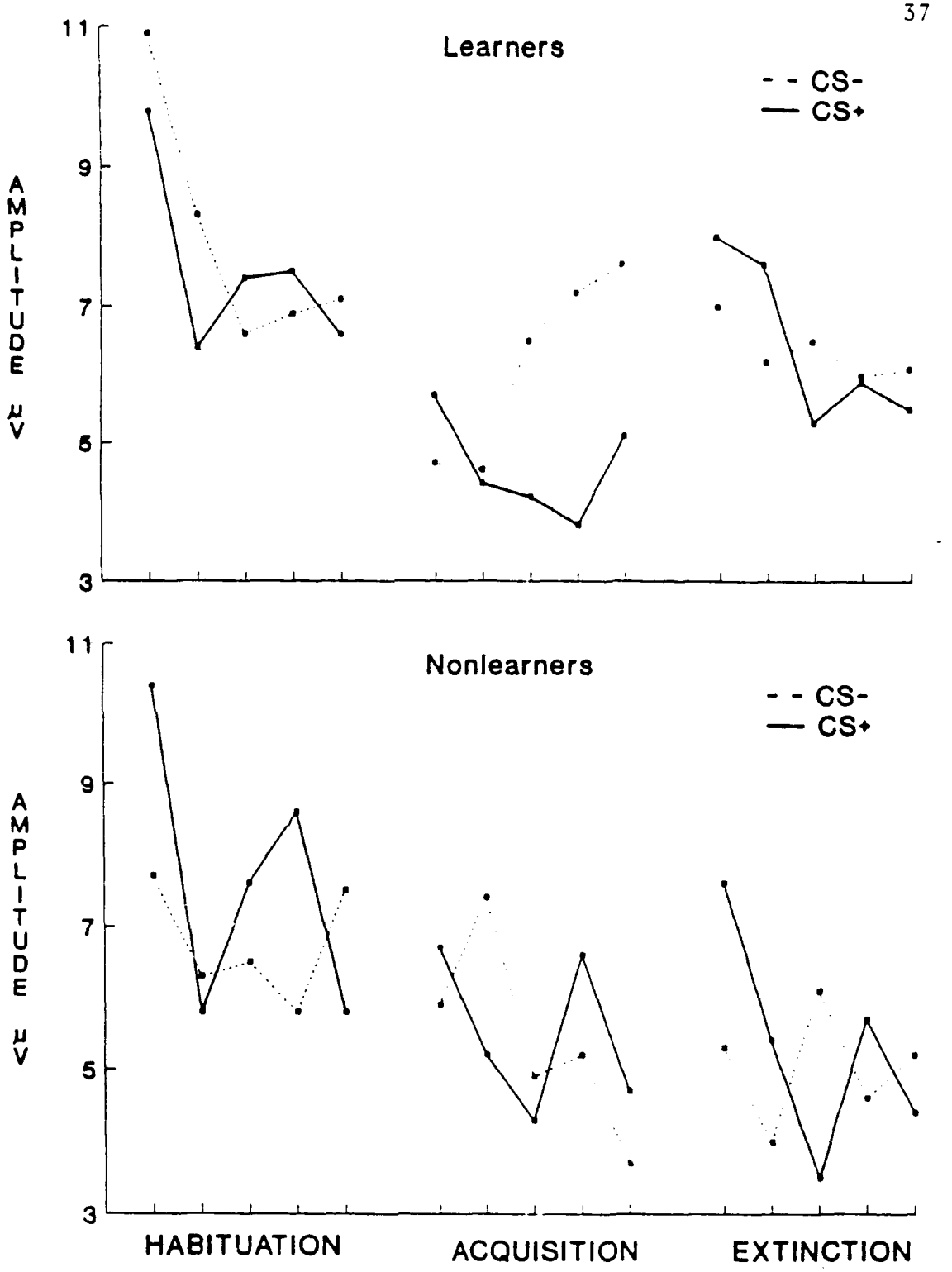


Figure 3 - P300 amplitude for learners and nonlearners across the three test phases

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6.4 Experiment 4 - Ultradian Rhythms in Performance and Evoked Potentials

Ultradian rhythms are biological rhythms with frequencies greater than one per day. Research has focussed on URs with a period in the range of 60-140 minutes. This study assesses ultradian rhythmicity in event-related cortical activity and measures of human performance. Specifically, the following questions are addressed:

(1) Are there URs in ERPs?

(2) If so, what is the relationship between URs in ERPs and performance?

As indices of state-related changes in CNS functioning, the discovery of URs in ERPs would be of interest in itself. Additionally, the demonstration of rhythmicity in ERPs may provide information regarding the CNS processes underlying performance variability. Further, a relationship between rhythms in ERPs and performance might indicate their usefulness as a predictive tool in evaluating performance readiness.

URs have been found in a number of behavioral and physiological variables. Their relationship, however, is not clearly understood. Because they are viewed as indices of such constructs as arousal, attention, and cognitive processing, ERPs are well-suited as a psychophysiological measure for the investigation of CNS correlates of performance variability.

To investigate the nature of the relationship between URs in ERPs and performance, a RT task is used. The traditional behavioral measure of decision latency has been reaction time, and there is research investigating ERP components (N200, P300) as indices of decision latency. Although behavioral validation of hypothesized cognitive processes associated with ERPs is important, past studies often failed to include RT measures. For those studies which did, the results have been equivocal. The relationship between P300 and RT appears to be stronger when the focus is accuracy rather that speed (Donchin et al., 1986). Ritter et al. (1979) suggested that the decisional processes associated with RT may have a stronger relationship to the N200 component. Globus and Lavie (1980) found no rhythm in movement time, when accuracy rather than movement time was the focus. They suggested that only task parameters which are attended will reveal ultradian rhythmicity. To investigate state-related changes in responding, this study attempts to maximize the normally occurring biological rhythm by placing no special emphasis on either speed or accuracy. The focus of the study is the N100, N200 and P300 components. N100 has been shown to be influenced by general levels of alertness (Naatanen & Picton, 1987), and several studies have shown a relationship between N200 amplitude and RT (e.g., Bostock & Jarvis, 1970; Naatanen & Gaillard, 1974). N200 amplitude was larger when RT was shorter. The other two components are considered to be influenced by alertness, attention, and cognitive processing. Like N100, N200 amplitude has also been correlated with RT, but in a reverse

manner. Larger N200 deflections were associated with longer RTs (Wilkinson & Morlock, 1966). N200 latency has also been correlated with RT (Ritter et al., 1979). The P300 component has been shown to reflect state-related changes (e.g., Broughton & Aguirre, 1987) as well as demonstrate a relationship with RT measures (e.g., Ritter et al., 1972).

METHOD

Subjects Eight male subjects, ages 18-30 (mean=24.5), were recruited from the student population of the University of Southern Mississippi. Subjects were screened for cigarette smoking, medication use, health problems, excessive caffeinated-beverage consumption, or ill effects (e.g., headaches) due to abstention from caffeinated beverages (see Appendix A for subject interview questionnaire). Subjects were paid $75 for their participation in the study.

Apparatus

Event-related potentials Subjects were tested in a 9 ft x 13 ft room. Grass gold-cup electrodes were attached to the scalp with electrode paste (impedances not exceeding 5,000 ohms). ERPs were recorded from Fz, Cz, and Pz locations (International 10-20 Electrode Placement System; Jasper, 1958) and referenced to linked mastoids. EEG was recorded from C4 and O1 and observed for signs of sleepiness in accordance with standard sleep scoring methods (Rechtschaffen & Kales, 1968). EOG was also recorded for subtracting eye-blink artifact from the averaged evoked potential measures by a computer algorithm (Gratton, Coles, & Donchin, 1983). Auditory stimuli were presented binaurally through headphones, using a Bernoulli series of randomly occurring tones. Target tones (p=.10) were set at 2000 Hz frequency and nontarget tones (p=.90) at a frequency of 1000 Hz, with a tone duration of 50 msec and a rise/fall time of 5 msec. Stimulus intensity was 60 dB (SPL), and the interstimulus interval was one second.

Tone presentations were controlled by Coulbourn Instruments solid state equipment. The EOG and the EEG signals for the ERPs were amplified by Coulbourn High-gain Bioamplifiers with high-pass filters set at 1 Hz, low-pass filters at 40 Hz, and gain at 10,000. Amplified signals were digitized and stored at 200 Hz on a Compaq 386-25 microcomputer using a Data Translation DT2821 A-D board. EEG signals for monitoring sleepiness were recorded on a Grass Model 78-D polygraph.

Reaction time An AT&T 6300 microcomputer recorded reaction times using a Data Translation DT2801 A-D board. The computer was programmed to poll the A-D channel at a rate of 200 Hz which resulted in a maximum error of 5 msecs in detection of a response. Reaction time was measured by a device strapped to the preferred hand of the subject. The device consisted of a board with straps to hold the subject's hand in a position of performance readiness and photobeam and photoreceptor cells positioned above the subject's fingers. All but the subject's index finger was secured by a strap. Upon detection of the target tone, the subject lifted his index finger to break the photocell light beam. This triggered the recording of reaction

time by the computer.

Procedure

Subjects were tested on weekends and holidays in a room free of all time cues (i.e., no clocks, watches, or windows, and a constant level of light). In addition, subjects were not informed of time elapsed or time remaining in the test period. Subjects reported to the Sleep Research Laboratory the day prior to testing, at which time experimental procedures were explained, written consent (see Appendix C) was obtained, and three practice sessions were administered. Subjects received the following instructions:

You will be listening to a series of low and high- pitched tones. You are to ignore the low tones and pay attention only to the less frequent, high-pitched tones. When you hear the high tone, count it - not out loud, but to yourself mentally - and at the same time lift your index finger as quickly as you can to break the photobeam. While you are performing the task, keep your eyes open, focus on a spot in front of you and try not to blink during tones. If you feel the need to blink, try to blink between tones. However, don't worry about blinking so much that you cause your eyes to bother you. This will only increase your desire to blink. At times you may feel drowsy. Do not fall asleep; try to remain awake, pay attention, and respond as quickly as you can. If you are having difficulty staying awake, you will be prompted to stay awake and continue responding to the high tones. In addition, subjects were instructed to refrain from alcoholic beverages the night before testing, to get a good night's sleep, and to refrain from eating breakfast or drinking coffee prior to reporting for testing, as food would be provided in the lab.

The day of testing subjects received a wake-up call from the experimenter an hour prior to reporting for the experiment. Subjects reported individually to the Sleep Research Laboratory at 08:30. After electrode hookup the subject was seated in a recliner chair in the testing room, experimental procedures were reviewed, and testing began. The total testing period lasted for eight hours with each trial commencing every 15 min and lasting approximately 5 min. The total number of tones presented in each trial was sufficient to obtain 30 randomly-presented target tones at 10 percent probability (i.e., approximately 300 total tones). RT and ERP measures were recorded for both target and nontarget stimuli and stored on computer for later off-line analyses. EEG was recorded on paper.

A constant routine (Minors & Waterhouse, 1984) was maintained throughout the testing period. It consisted of the subject remaining in the same semi-reclining position, arising only when necessary. Small, measured amounts of food and non-caffeine liquids, chosen in advance by the subject from a limited menu (see Appendix D), were provided to the subject at regular hourly intervals. Between trials, in addition to eating, the subject read selected materials, studied, or talked with the

experimenter or research assistant. During each trial EEG was monitored for signs of sleepiness, and when they occurred, the subject was prompted, at the beginning of the next trial, to stay awake and pay attention to the task.

RESULTS

ERPs After correction of each individual evoked potential using a computer algorithm for removal of eye-blink artifact (Gratton et al., 1983), both target and nontarget ERPs were averaged to obtain 33 separate waveforms (corresponding to the 33 15-min time intervals of the study) for each of the three electrode placements (Fz, Cz, and Pz). Averaged ERPs were then baseline-adjusted by subtracting the average of the first 30 points (a 150 msec prestimulus baseline) from each of the remaining 170 points. From this adjusted waveform, peaks were then scored by a computer program which picked the lowest or highest peak within a specified time window. Although the focus of the study is N100, N200, and P300 components, all peaks were scored for latency and amplitude using the following windows: P100 - 10-70 msec; N100 - 70-140 msec; P200 - 140-200 msec; N200 - 170-250 msec; P300 - 230-500 msec. Scored ERPs were checked for poorly formed peaks or ones which occurred outside the computer-scoring windows. These were scored by the experimenter by visual inspection. One subject (subject 5) had unusually long latencies for some components. For this subject, all peaks were scored by the experimenter using the visual scoring method. For all subjects, the P100 component was found to be often too poorly formed to reliably pick a peak either visually or by computer; therefore, no further analyses were done on this component.

A random check of each subject's scored waveforms was made to compare the ERPs from the three leads for a general similarity in their waveforms. Overall, these were found to be morphologically similar. The data of Subject 8 (Figure 1) is representative. Amplitude was generally maximal at the Cz lead, and all further analyses were performed with the data from Cz lead only.

Eight 33-point time series per subject were constructed from the amplitude and the latency values for each of the N100, P200, N200, and P300 components, for a total of 64 series. They were plotted for visual inspection. The data of Subjects 1 and 4 illustrate the rhythmicity found in the undetrended data (Figures 2 and 3). Each subject demonstrated rhythmicity in various ERP measures, but there were often wide differences as to which measures showed rhythmicity and the frequency at which they oscillated.

Nonstationarity is indicated by the linear trend line in these figures. In some cases, however, quadratic and cubic trends were present; consequently, the time series were submitted to polynomial regression. Regression analysis was used to correct nonstationarity in the data by subtracting third degree polynomials. Residuals after removal of the polynomials were submitted to power spectral analysis (BMDP1T), which produced

spectral density estimates for 17 frequencies. All spectral density estimates were converted to percent of total variance at each frequency. Percentages at the different frequencies were averaged across the eight subjects and then plotted.

The following test for statistical significance was performed on the averaged data. Based on the assumption of a randomly distributed variable, an equal proportion of variance would be expected to occur at each frequency, with the exception of the zero and the fundamental frequencies (0.0 and 2.9 cpd). These frequencies are associated with trends and curvilinearity in the data that was removed prior to spectral analysis by subtracting third degree polynomials. An equal proportion of variance for each of the remaining 15 frequencies was calculated to be 6.667 percent for a random variable. Next, the actual proportion of variance at the five frequencies which correspond to the period of Kleitman's (Kleitman, 1963) BRAC (i.e., 62-124 min or 11.6-23.3 cpd) was summed. In this theoretical band of interest, the proportion of variance that might be expected to occur with a randomly distributed variable was approximately 33.33 percent (5 X 6.667). The t statistic was used to test whether the proportion of variance actually occurring in the BRAC frequency band was significantly different from the 33.33 percent expected to occur randomly. This procedure was performed separately for all of the ERP measures. Table 1 presents the averaged percent of variance accounted for at the 17 frequencies for the ERP measures and the mean RT measure, which is discussed separately below.

Latency Figure 4 presents the variance spectra for the latency measure for N100, P200, N200, and P300 components. The variance accounted for within the theoretical band of interest was significantly greater than expected by chance for N100 latency (40.5 percent; $t[7]=6.11$, $p<.0005$) and N200 latency (42.7 percent; $t[7]=5.601$, $p<.0005$). The proportion of variance accounted for within the theoretical frequency band was not significant for either P200 latency ($t[7]=-1.065$, $p>.05$) or P300 latency ($t[7]=-4.472$, $p>.05$). However, in several cases spectral peaks in the P300 latency data of individual subjects indicated rhythmicity. For example, Subject 8 had 54.4 percent of power in the range of 45-71 min. Other subjects had power split between primary and secondary peaks, few of which were in the theoretical band (e.g., Subject 6 with peaks at 165 and 50 min).

Amplitude Figure 5 presents the variance spectra for the amplitude measure for N100, P200, N200, and P300 components. The proportion of variance in the theoretical band for N100 amplitude was significant (36.7 percent; $t[7]=2.92$, $p<.02$), as was that for N200 amplitude (35.5 percent; $t[7]=2.124$, $p<.05$). The proportion of variance found in the BRAC frequency band was also significant for P200 amplitude (35.4 percent; $t[7]=2.35$, $p<.05$). As with the latency measure, P300 amplitude was not significant averaged across subjects ($t[7]=1.736$, $p>.05$), but the data of individual subjects showed rhythmicity. Four subjects demonstrated

rhythmicity at the BRAC frequency, while the data of the other subjects reflected faster activity. For example, Subject 8 had 57.3 percent of the variance within the 62-124 min band, while Subject 3 had 52.5 percent of the variance in the 45-71 min range.

Reaction Time Due to equipment problems RT was not recorded for every target. The problem was determined to have occurred randomly, however, and therefore not deemed to bias the reaction time data. The mean number of RT measures available per trial for averaging was 16.

Three measures of reaction time for each trial were calculated: (1) mean RT; (2) the mean of the five slowest RTs; and (3) the median RT. Median RT showed very little variability; consequently, no further analyses were performed with this measure. Two 33-point time series per subject were constructed from the averaged RTs and the average of the five slowest RTs and plotted for visual inspection. The data of subjects 3 and 5 illustrate the rhythmicity found in the undetrended data for the averaged RT measure (Figure 6).

The 16 time series for RT and 5 slowest RT were corrected for nonstationarity by subtracting third degree polynomials. As with the ERP data, third order residuals were submitted to power spectral analysis, producing spectral density estimates for 17 frequencies. Finally, spectral estimates were converted to percent of total variance accounted for at each frequency (see Table 1).

Figure 7 presents the spectra for the mean of all RT scores and the mean of the five slowest RTs. The two spectra are essentially the same; however, there is more power at the BRAC frequency for the mean of all RTs (41.6% compared to 38.1%). As no additional information is provided by the mean of the five slowest RTs, no further analyses were performed with this measure. Percent of variance accounted for within the theoretical band (11.6-23.3) for the mean RT measure was tested for significance using the t statistic in the manner described above with the ERP measures.

ERP/RT Relationship Prior to analysis of the ERP/RT relationship visual inspection of the ERP and RT spectra revealed, in addition to the rhythmicity within the theoretical range, some relatively fast activity in most of the ERP measures (see Figures 4-5). As this faster activity could mask the ERP/RT relationship in the band of interest, the time series were smoothed with the von Hann numerical filter prior to analysis. This filter applies a moving average across three adjacent values with coefficients of .25, .50, and .25. In addition to removing the fast cycles in the data, this also results in attenuation in the amplitude of the five frequencies in the band of interest. However, all series were attenuated equally. Figure 8 presents the frequency response curve for the filter. In the five frequencies representing the 62-124 min period attenuation ranges from eight percent (in the slowest frequency) to 38 percent (in the fastest frequency) with a mean of 22 percent.

The relationships between reaction time and the different ERP measures were analyzed by cross-correlation (BMDP2T). When averaging the correlation coefficients across subjects, the wide variability in period and phase among subjects reduced the ERP/RT relationship that was evident in individual subjects. Consequently, cross-correlations are described in terms of individual subjects. Figures 9 through 16 present the cross-correlation functions (CCFs) at plus and minus 30 lags, arranged by subject. Coefficients at negative lags represent correlations with the ERP series lagged, and coefficients for the positive lags represent those with the RT series lagged. Table 2 presents critical r values for a two-tailed test, .05 level of significance, for lags zero through sixteen. No correlations beyond the sixteenth lag were significant. For ease in viewing the ERP/RT relationship by component, CCFs are additionally organized by ERP measures (Figures 17 through 23).

The CCFs revealed the following:

1) ERP measures were related to reaction time. Symmetrical CCFs can be seen in all subjects, often in several measures. Correlation coefficients were as high as .74, and significant correlations often demonstrated a repeating pattern within a particular measure.
2) One of the most striking findings was that of individual differences. No one ERP measure best correlated with RT. Rather, some measures demonstrated symmetrical functions for some subjects, while other measures were better correlated for other subjects.
3) Inspection of CCFs by ERP measure (Figures 17-23) suggests that the N100 and N200 components were most strongly correlated with RT. N100 in particular had well-shaped CCFs in at least six of the eight subjects for both the latency and amplitude measures. Moreover, when the latency measure did not appear to be related to RT, the amplitude measure did. With the exception of one subject (No.8), this held true for N200 as well.

The correlation coefficients at the zero lag of the CCFs represent the simple correlations between RT and the different ERP variables. These coefficients are presented in Table 3. Significance was found for the mean correlation of RT and N200 amplitude (r=.175; $t[7]$=2.035, $p<.05$). Significant one-tailed correlations in individual subjects for different measures at zero lag are also indicated in Table 3. One-tailed tests were used to assess several hypotheses generated by the ERP/RT literature. These are discussed below.

DISCUSSION

The purpose of this study was to assess ultradian rhythmicity in event-related cortical activity and in performance. In addition, it explored the relationship between the rhythms in these two variables. The following general findings are reported:

1) URs were demonstrated in various ERP measures;

2) URs were demonstrated in reaction time;
3) a relationship between rhythms in ERP measures and rhythms in RT was demonstrated;
4) there were wide interindividual differences as to the ERP measures which best demonstrated rhythmicity and inter and intraindividual differences in the dominant periods for the various measures;
5) there were interindividual differences as to which ERP measures best demonstrated a relationship with RT, as well as interindividual differences in period and phase of the ERP/RT relationship.

Ultradian Rhythms in ERPs The rhythmicity in both latency and amplitude for the N100 and N200 components was statistically significant. For both components, however, latency had more clearly-defined spectral peaks (Figure 4), compared to the amplitude spectra (Figure 5) where power was more widely distributed across the frequencies. For P200 amplitude, which was statistically significant, power was also widely distributed across frequencies, while the P200 latency measure was not statistically significant.

Although a significant amount of variance was not found in the theoretical band for either latency or amplitude in the averaged spectral values for the P300 component, inspection of the spectra for individual subjects revealed rhythmicity in many cases. P300 amplitude in particular demonstrated rhythmicity in individual subjects. Wide variability in individual spectral peaks accounted for the lack of significant rhythmicity in the theoretical band when spectral estimates were averaged across subjects. This observation highlights a sometimes problematic characteristic of time series analysis.

Although averaging across subjects can improve stability of the spectral estimates, it may obliterate spectral peaks in highly variable measures. Consequently, the importance of perusing individual spectra should not be overlooked. In addition to indicating rhythmicity that would be lost in the averaging process (i.e., as with P300), inspection of individual spectra also revealed that averaging often greatly reduced spectral power for the various measures. For example, with Subject 7 the amount of variance accounted for in N100 amplitude in the 62-124 min band was greater than 55 percent, while averaging across subjects resulted in 36.7 percent. Some subjects demonstrated similarly strong rhythmicity outside the BRAC frequency band. For example, N100 amplitude for Subject 4 had 57.4 percent of the variance within the 41-62 min range. Individual inspection also revealed that in addition to power at primary peaks, some subjects had secondary peaks. It is difficult to interpret whether these additional peaks are bona fide secondary periodicities or the result of deviations in the data from a purely sinusoidal shape, 'leakage' from the slower frequencies, or the power from faster frequencies which lie outside the sampling rate of the analysis and are 'aliased' to frequencies within the bounds of the analysis (Bloomfield,

1976). Of interest is the temporal relationship between the various ERP component measures. A range of 60 to 120 min best described the BRAC period as discussed in the ultradian literature. Consequently, statistical tests for significance were done on the basis of 62-124 min (the corresponding periodicity represented in these data). However, these boundaries represent tendencies in the data, and both slower and faster activity have been reported. While the temporal center of the BRAC period for this study was approximately 83 min, all of the ERP measures which showed significant power in the theoretical band had spectral peaks indicating faster rhythms. N100 latency and amplitude, P200 amplitude, and N200 latency all peaked at 71 min. N200 amplitude had a 55-min peak, i.e., outside the theoretical window. While P300 latency was not statistically significant within the BRAC band, it had, in addition to a nonsignificant peak at 165 min, a significant peak at 55 min ($t[7]=1.933$, $p<.05$).

To some extent this difference in dominant peaks may be determined by the limits of the statistical procedure. There is poor resolution between the frequencies at the 'slow end' of the spectrum when the number of points in the time series is relatively small. In this study, for example, power could be expressed at either 83 or 99 min when in reality oscillations may have resembled more closely 90 min cycles. However, given this caveat regarding statistical limitations, it is noteworthy that all ERP measures demonstrated activity somewhat faster than the average BRAC frequency. This difference may reflect the fact that ERPs are a measure of CNS activity. Most measures demonstrating ultradian rhythmicity have been peripheral psychophysiological measures, such as heart rate or urine composition, or performance measures, which involve both central and peripheral mechanisms. ERPs are more closely related to the initial processes involved in perceiving and evaluating stimuli.

Of further interest are the differing periodicities within the ERP measures themselves. N100 latency, N100 amplitude, P200 amplitude, and N200 latency demonstrated the same 71-min periodicity, while N200 amplitude and P300 latency had periods of 55 min. It is possible that these differences reflect the exogenous/endogenous component dichotomy. There are several characteristics which differentiate these categories. The exogenous components (00, P200) are more closely related to sensation and perception and are far less variable in latency than the later endogenous components (N200, P300), which are considered to be indices of information processing. Comparing, for example, N100 and P300 we find that N100 latency typically occurs within a 50-msec window, while the latency window for the P300 component is approximately 300 msec. With stimulus characteristics held constant, the major factor influencing N100 is subject state. In other words, URs may appear as fluctuations in overall level of arousal. The P300 component, on the other hand, is additionally influenced by psychological factors such as attention and motivation.

Although N200 is typically identified as an endogenous component, N200 latency had the same period as the exogenous measures. The 'coupling' of the N200 latency measure with the N100 component may be the result of the MMN. The MMN, elicited by a deviant stimulus, is a broad component that can overlap both the N100 and N200 components. While the MMN is not affected by attention (an endogenous factor), it does vary with differences in arousal level (Sams, et al., 1983). The discovery of URs in ERPs with awake adult subjects is an important finding with respect to rhythmical variations in event-related potentials. Due to the paucity of research in the area, no direct evidence of URs in ERPs existed for this population. Previous research either demonstrated diurnal variation with sampling rates insufficient to establish ultradian rhythmicity (Broughton & Aguirre, 1987; Harsh & Badia, 1989), or changes in ERPs during sleep (Tanguay et al., 1973) or immediately following arousal from different stages of sleep (Broughton, 1968). If the cyclicity of REM sleep is a sleep-dependent phenomenon as purported by Moses et al. (1977), rather than the sleeping manifestation of an ongoing BRAC (Kleitman, 1963), then the findings of URs during sleep cannot be generalized to waking populations. The generalizability of results from ERPs collected immediately following arousals from sleep is also questionable. In addition, subjects were either children, narcoleptics or sleep-deprived individuals, making generalization from these earlier studies to a normal adult population impossible.

In addition to the demonstration of ultradian rhythmicity in waking ERPs, the present study also provides confirmation of the slower diurnal trends that have been seen in previous studies (Browman, 1979; Harsh & Badia, 1989). Although the data were detrended prior to spectral analysis because the focus of this study was ultradian rhythmicity, diurnal trends were present in the data of most subjects (see Figures 2 and 3).

Ultradian Rhythms in RT RT clearly demonstrated ultradian rhythmicity in this study. Power spectral estimates were more stable for this measure than most of the ERP measures, with all subjects having either primary or secondary peaks within the BRAC band. In addition, the period for RT was consistent with the BRAC literature on performance measures, as evidenced by the clearly-defined spectral peak at 99 min (Figure 7).

These data support Lavie's (1982) observation that task parameters and experimental design may play a role in the manifestation of ultradian rhythmicity. Lavie's adaptive serial RT task and the provision of feedback in the Gopher and Lavie (1980) study seemed to modulate rhythmicity in performance. This study, on the other hand, replicated the findings of Stampi and Stegagno (1985) using the cognitively more demanding CRT task, as well as a protocol which held stimulus characteristics constant and placed no special emphasis on speed or accuracy. This lack of emphasis may account for the emergence of the relatively 'delicate' ultradian rhythm. Given the influence of experimental

design, the stability of this measure compared to most of the ERP measures is notable.

ERP/RT Relationship Although a relationship was demonstrated between changes in ERPs and changes in RT, the nature of the relationship was complex, with individual differences being a striking feature of the data. Overall, the N100 and N200 components seemed to be most strongly related to changes in performance. For N100 latency (Figure 17), seven of the eight subjects, and for N100 amplitude (Figure 18), six of the subjects, had fairly symmetrical CCFs. For N200 latency (Figure 19), five subjects, and for N200 amplitude (Figure 20), at least six subjects, had symmetrical functions. In all cases, however, there was such wide variability in period and phase, coefficients could not be averaged across subjects without the loss of a significant amount of information. While the evidence is not conclusive, the strong relationship between the N100 and N200 components and RT suggests the possibility that the MMN is actually the component that best predicts performance. Further evidence for this conclusion may be indicated by the P200 amplitude measure which should also be influenced by the MMN due to its location between the N100 and N200 deflections. CCFs for P200 amplitude were also well-formed (Figure 21).

Although analysis of the ERP/RT relationship focussed on cross-correlation and the shape of the CCFs, several other methods provided additional information. One of these was a comparison of the ERP and RT periods. The exogenous components (00, P200) with a period of 71 min, and the endogenous components (N200, P300) with a period of 55 min, demonstrated somewhat faster activity than RT (99 min period). Once again bearing in mind the statistical limitations of the analysis which make an exact determination of periodicity impossible, these data suggest that the nature of the measures played a role in generating different periodicities. While ERPs are measures of CNS activity involving processes such as sensing, perceiving, stimulus evaluation, and decision making, responding is dependent on a complex of sensory, cognitive, and motoric processes. That the periodicity of the CNS measures was shorter than that of RT may indicate that changes in CNS state occurred prior to changes in performance. In other words, reductions in arousal may not be simultaneously accompanied by performance deterioration. It is possible that as reductions in arousal occurred subjects were able through some compensatory mechanism, either motivational or motoric, to sustain performance levels for a time. This process may lengthen the period of the performance measure.

Another source of information was the simple correlations between RT and the ERP variables (see Table 3). Ritter et al. (1979) proposed that N200, rather than P300, latency was an index of decision-making. Under the Ritter hypothesis, N200 latency and RT should be positively correlated. These data provided some support of this claim. While the mean correlation for RT and N200 latency ($\underline{r}$=.175) was significant ($\underline{t}[7]=2.035$; $p<.05$), the mean correlation for RT and P300 latency ($\underline{r}$=.121) was not.

However, for the RT/N200 latency relationship, although all but one subject had positive correlations, only three of the individual correlations were significant. For the RT/P300 latency relationship, three subjects also had significant positive correlations, but several subjects had negative correlations.

Other findings were not supported. Several studies (e.g., Bostock & Jarvis, 1970; Naatanen & Gaillard, 1974) found that RT was shorter when N100 amplitude was larger. While four of the eight subjects in this study had negative N100 amplitude/RT correlations, only one was significant (r=-.726, $p<.005$), and the mean correlation (r=-.026) was not significant. Nor was a finding of a positive relationship between N200 amplitude and RT (Wilkinson & Morlock, 1966) supported by this study. Only two subjects had significant positive correlations, and the mean correlation (r=.081) was nonsignificant.

Although no literature on the relationship between N100 latency and RT was found, these data indicated a strong relationship between the two variables. By hypothesizing a positive relationship (i.e., the longer it takes to sense/perceive the stimulus, the longer reaction time should be), significant correlations were found for four subjects, but the mean correlation for all subjects (r=.139) was not significant. However, it can be seen from Table 3 that this was due to the large negative correlation of one subject (r=-.677). It is possible that this subject attempted to compensate for waning arousal by emphasizing response speed. Without this subject, the mean correlation for RT and N100 latency (r=.256) was significant ($t[6]$=3.82; $p<.005$).

Implications for the BRAC Hypothesis These data reflect the complexity of the processes underlying ultradian rhythmicity. They do not resolve the debate over single vs. multioscillatory mechanisms. Although the different periods in the various measures might indicate a multioscillatory answer, a single-mechanism explanation cannot be ruled out, as the different measures are related to different processes. The exogenous components, reflecting sensory processes, may be under stricter control of the biological mechanism, while the endogenous components, involving cognitive processes such as attention, may be more susceptible to distractions and/or motivational factors and therefore more loosely controlled. At the end of a chain of processes is responding. It begins with the initial sensory encounter of the stimulus and incorporates the various sensory and cognitive processes with motoric functioning. This complexity of processes in the performance measure may influence oscillatory control in various ways. In this study RT was seen to be a more stable measure with a longer period than the ERP measures.

Conclusion The results of this study indicate that a certain amount of variability observed in measures of CNS activity and performance is due to biological rhythms at the

ultradian frequency. It is suggested that this rhythmicity is manifested as fluctuations in general level of arousal. In addition, these data indicate that ERPs hold promise as a predictor of performance degradation. Future research is needed to explore this possibility. In particular the indication that the changes seen in the N100 and N200 components is the result of the MMN needs further investigation.

More information is also required to determine if differences in periodicity observed with the exogenous and endogenous components is meaningful. Because of the small number of subjects and the problem of defining periodicity, associated with relatively limited data points, conclusions with respect to this finding must be tentative. Replication of these results is needed.

The difference in period for the ERP measures and RT is an interesting finding which also needs further investigation. This finding is not only of theoretical interest but its replication might provide useful information with respect to prediction of performance from ERPs.

Finally, an unresolved statistical issue is the relationship between the number of data points and frequency resolution at the slow end of the spectrum, and its effect on periodicity. Future research should increase the data point to time period ratio in order to improve resolution. This may help to clarify questions about the periodicity of the measures. Elimination of the 'odd-ball' paradigm would reduce the time on each trial, thereby making it possible to sample more frequently within each hour. However, for studies investigating cognitive processes such as decision- making and ERPs as a predictor of performance degradation, this approach is not suitable, since the MMN and the endogenous components are generated by the odd-ball paradigm. Another way to increase sampling rate, more suitable for ERP/performance studies, is to change the target to non-target ratio from 10:90 to 20:80. This would also reduce sampling time in each trial and make it possible to sample more frequently.

On the other hand, these data indicate that elimination of the odd-ball paradigm would not pose a problem for studies focussing on ERPs as a physiological marker of the rhythm. The strong rhythmicity found in N100, which is more closely related to sensing and perceiving than to decisional processes, suggests that this component, when experimental parameters are held constant, is a good indicator of subject state and can serve as a marker of the biological rhythm. Studies investigating, for example, the relationship between ultradian rhythmicity in ERPs and other physiological measures might consider elimination of the odd-ball paradigm in order to increase sampling rate.

A final possibility is to lengthen the overall testing period. Although subjects were becoming mentally and physically fatigued towards the end of the eight-hour test period, this time could possibly be increased by as much as two hours before subjects became mutinous.

Table 1

Average Percent of Variance Accounted for at 17 Frequencies

cpd	N1Lat	N1Amp	P2Lat	P2Amp	N2Lat	N2Amp	P3Lat	P3Amp	RT
0.0	0.49	0.56	0.43	0.57	0.55	0.48	1.14	0.62	0.71
2.9	1.68	1.75	1.41	1.87	1.96	1.65	3.54	2.08	2.11
5.8	4.14	3.39	3.60	4.90	5.47	4.24	7.36	5.10	5.45
8.7	6.06	4.22	6.05	6.94	8.64	6.38	8.69	6.66	8.15
11.6	**6.99**	**5.13**	**6.93**	**6.39**	**8.82**	**6.56**	**6.94**	**6.32**	**9.10**
14.5	**7.55**	**7.04**	**6.51**	**6.04**	**8.24**	**6.38**	**5.14**	**6.48**	**9.68**
17.5	**8.87**	**8.18**	**5.94**	**7.34**	**9.16**	**6.86**	**4.85**	**7.68**	**9.38**
20.4	**9.31**	**8.28**	**6.11**	**8.25**	**9.28**	**7.52**	**6.07**	**7.68**	**7.56**
23.3	**7.78**	**8.08**	**6.46**	**7.42**	**7.21**	**8.14**	**7.42**	**6.95**	**5.86**
26.2	6.26	7.81	6.26	6.24	5.25	8.46	7.51	6.60	5.64
29.1	6.43	7.94	5.51	6.34	4.32	7.75	7.07	6.10	5.94
32.0	6.01	8.20	5.62	7.27	3.80	6.47	6.58	5.46	6.47
34.9	5.01	7.73	6.06	7.72	4.15	6.14	6.34	6.52	6.26
37.8	4.94	5.89	6.69	6.53	5.26	6.29	5.61	7.53	5.43
40.7	5.17	4.91	7.76	5.91	6.02	6.58	5.01	6.95	4.45
43.6	5.95	4.92	9.10	5.13	6.05	5.72	5.03	5.82	4.72
46.5	7.34	6.38	9.58	5.14	5.82	4.46	5.71	5.46	3.10

Boldface type represents the BBAC frequency band.

Table 2

Critical *r* Values for .05 Level of Significance, Two-tailed

Lag	df	*r*
0	31	.344
1	30	.349
2	29	.355
3	28	.361
4	27	.367
5	26	.374
6	25	.381
7	24	.388
8	23	.396
9	22	.404
10	21	.413
11	20	.423
12	19	.433
13	18	.444
14	17	.456
15	16	.468
16	15	.482

Table 3

Correlations at Zero Lag

SUB #	N1LAT/RT	N1AMI/RT	N2LAT/RT	N2AMP/RT	P3LAT/RT	P3AMP/RT
1	.088	-.106	.488*	.250	.316*	-.326*
2	.218	.259	.062	.276	.300*	-.130
3	.426*	.261	.495*	-.340	-.121	-.496*
4	.406*	.170	.307*	.404*	-.076	-.298*
5	-.052	-.185	.035	.497*	.392*	.284
6	.376*	-.726*	.161	-.595	.211	-.227
7	.327*	-.196	-.254	.088	-.148	.064
8	-.677	.318	.146	.065	.096	.265
Mean	.139	-.026	.175**	.081	.121	-.108

* r is significant wich 1-tail test; $p < .05$
** t is significant with 1-tail test; $p < .05$

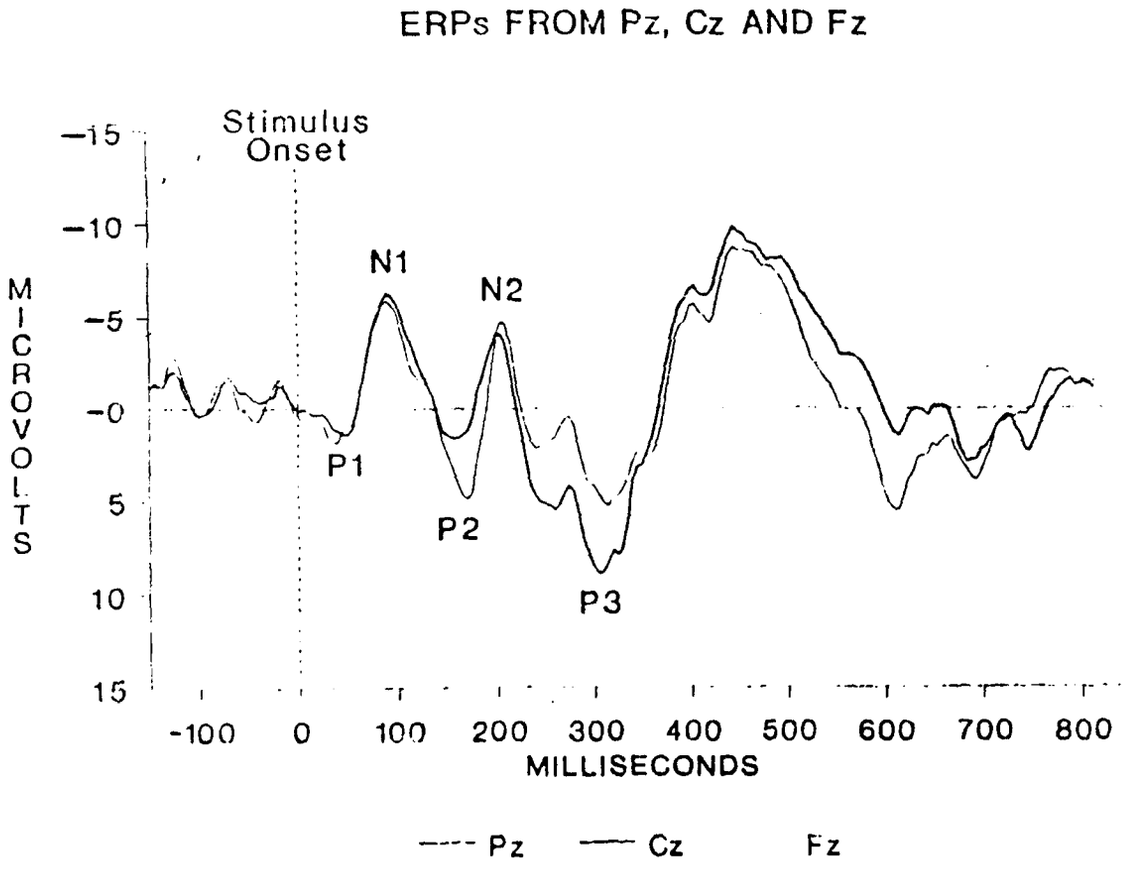


Figure 1 - ERPs from Pz, Cz, and Fz leads (Subject 8)

SUBJECT 1

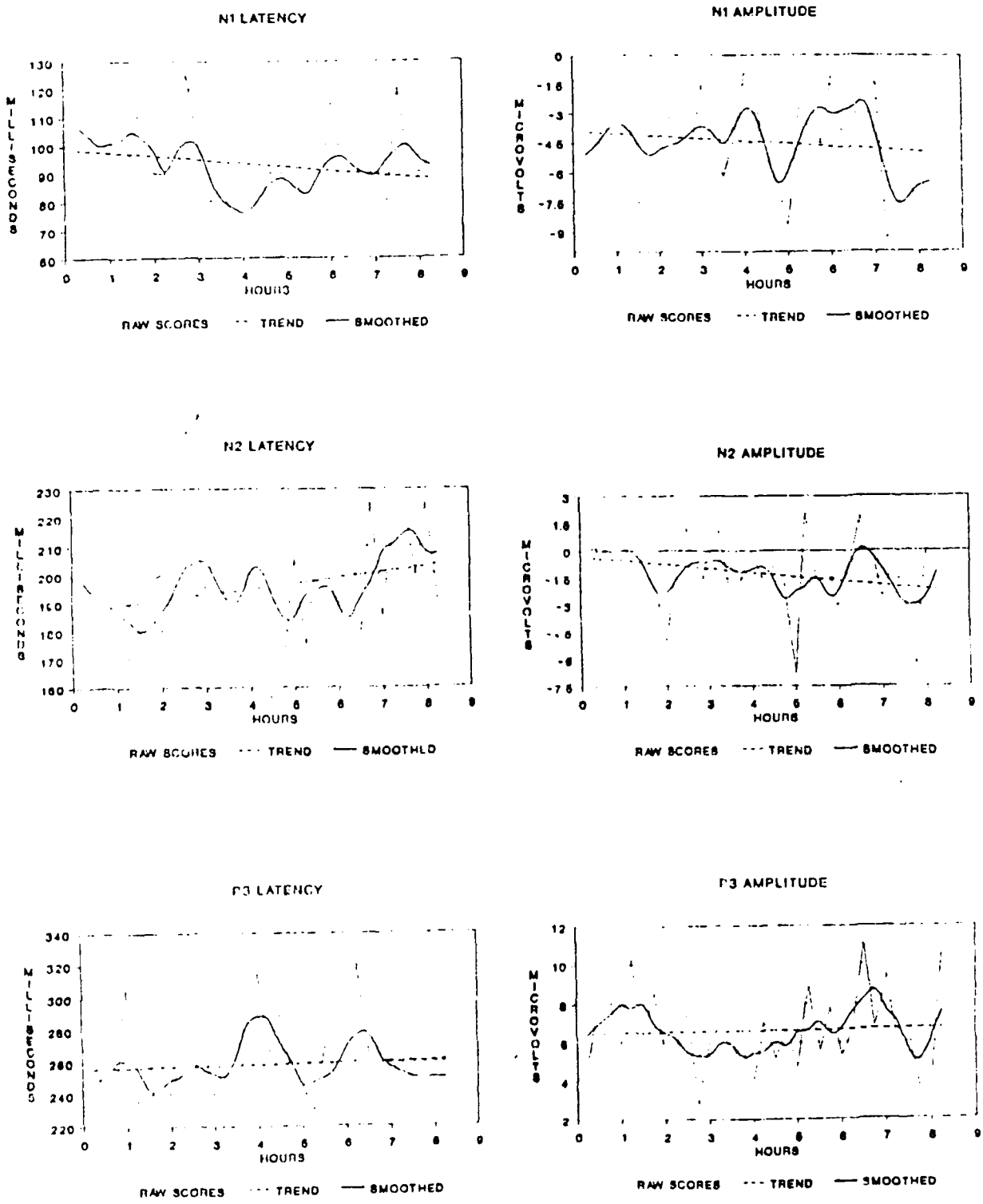


Figure 2 - Time series data for N1, N2, and P3 latency and amplitude (Subject 1)

SUBJECT 4

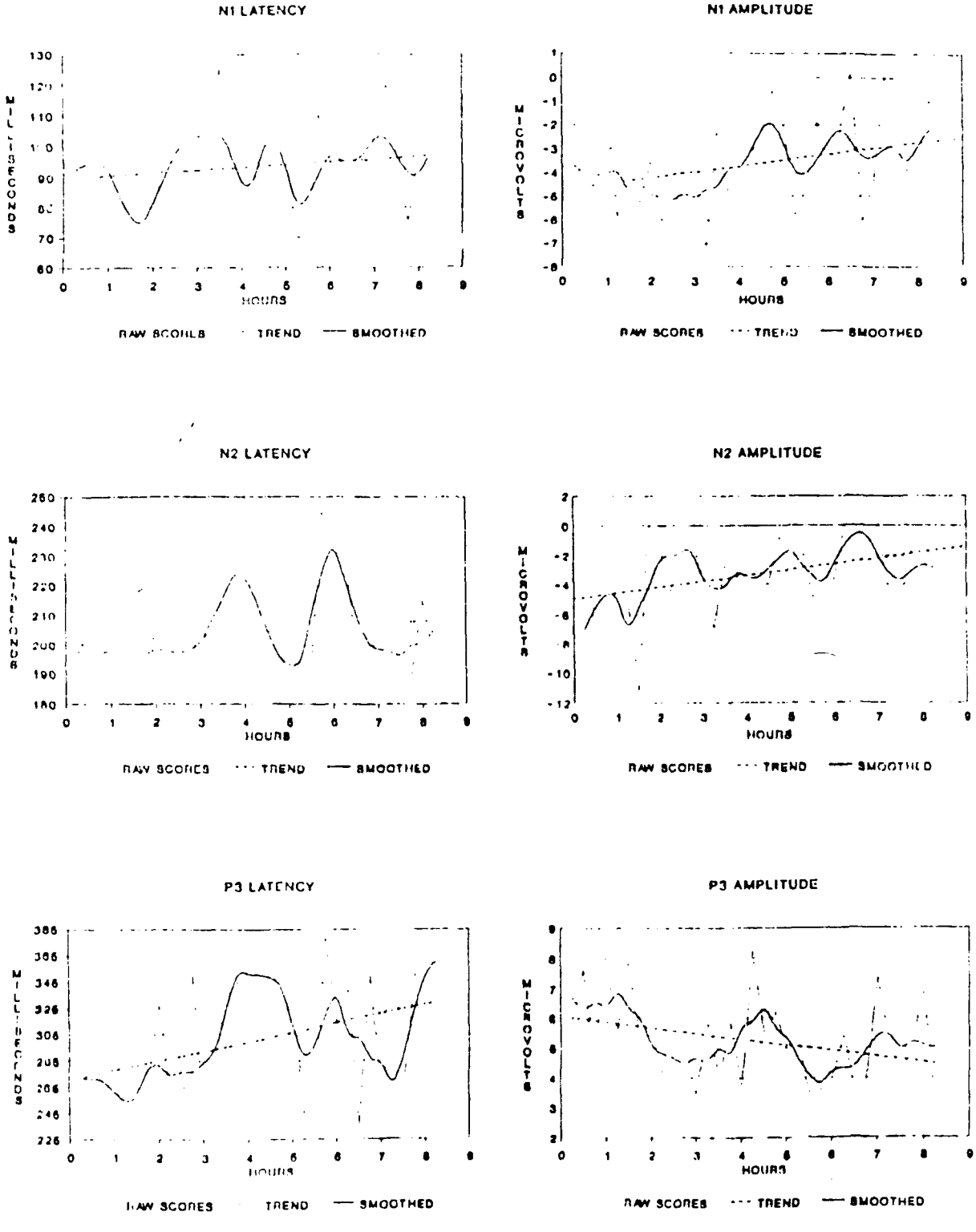


Figure 3 - Time series data for N1, N2, and P3 latency and amplitude (Subject 1)

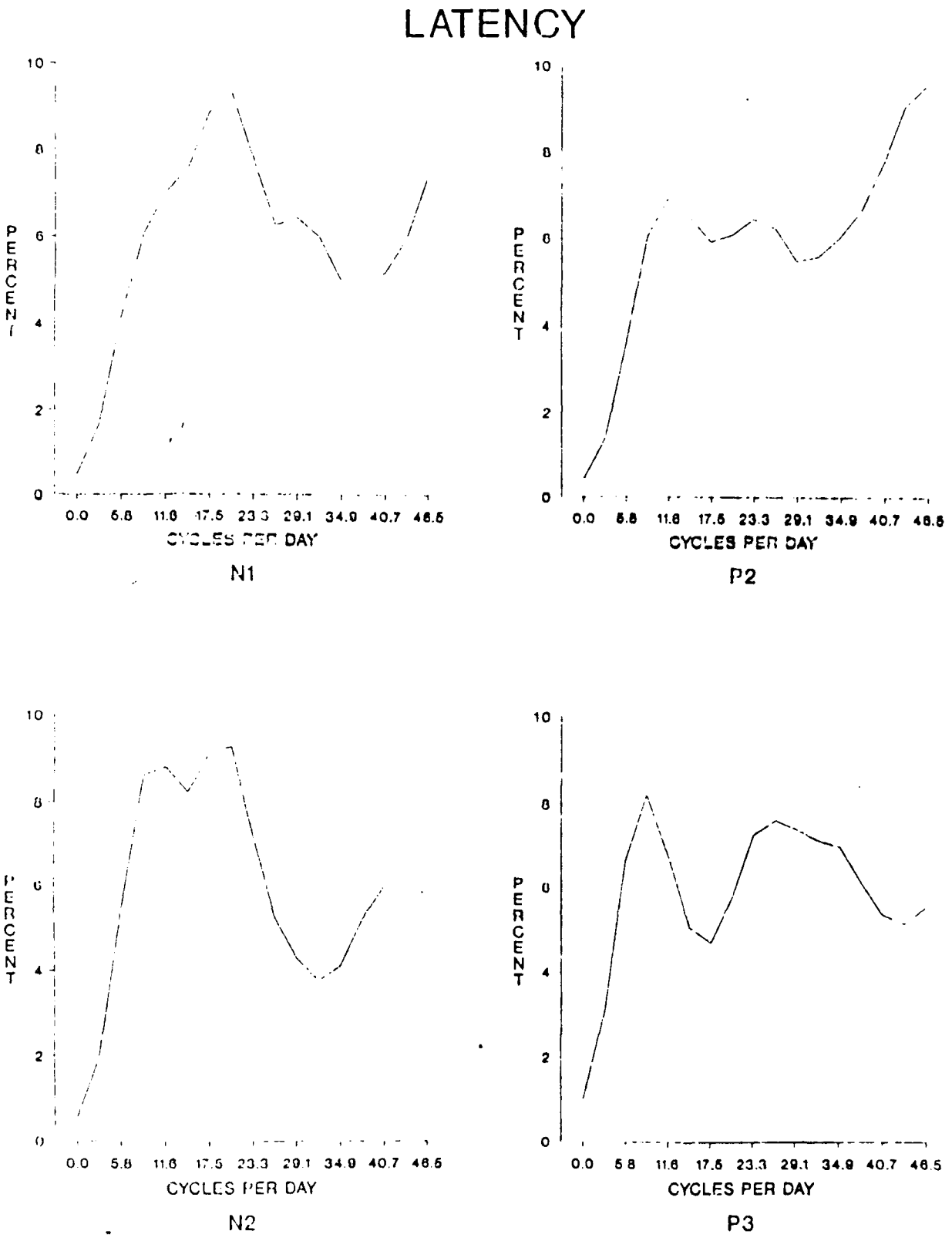


Figure 4 - Latency spectra (averaged across 8 subjects)

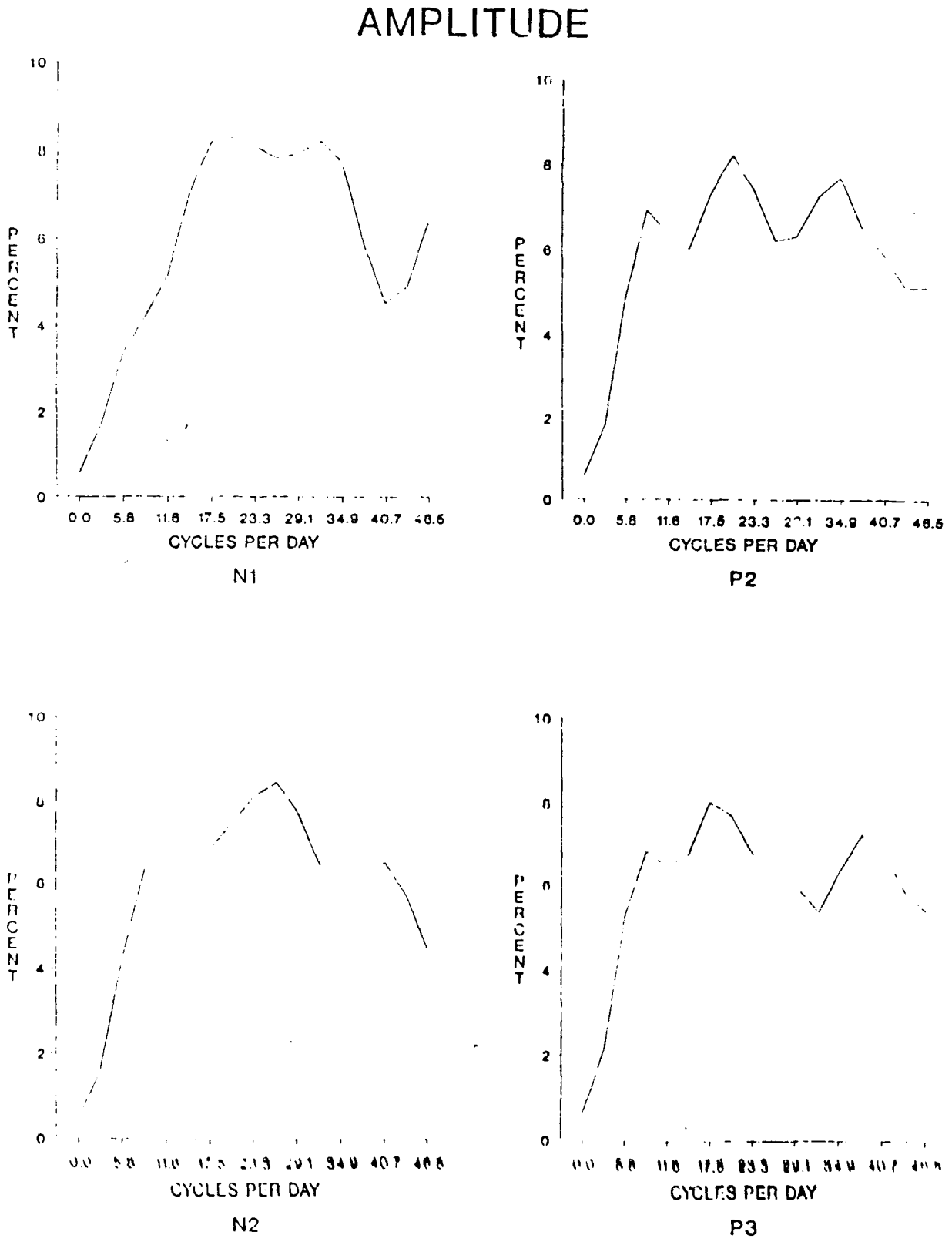
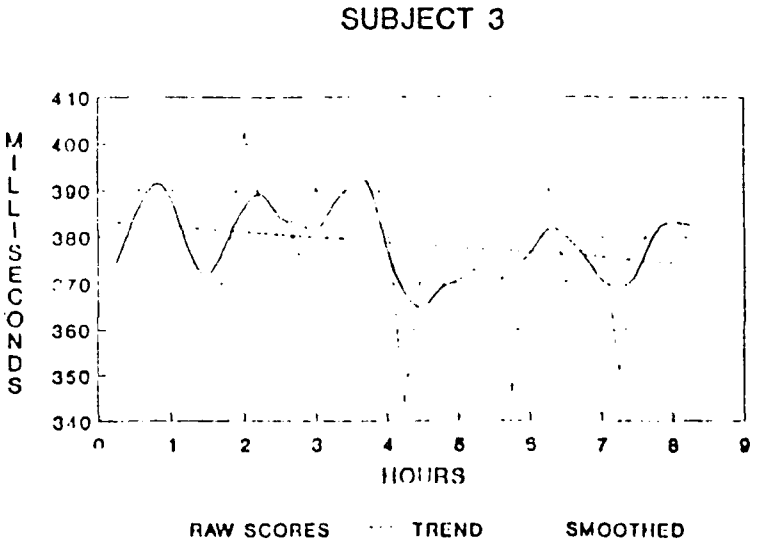


Figure 5 - Amplitude spectra (averaged across 8 subjects)

REACTION TIME



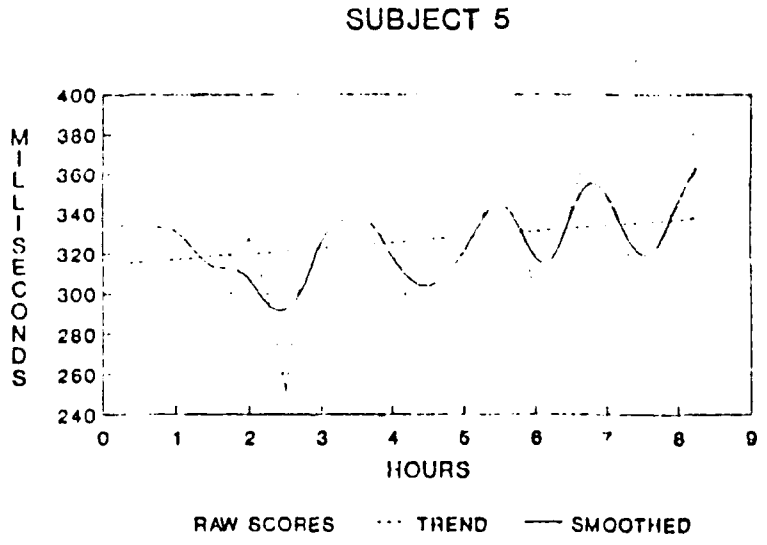
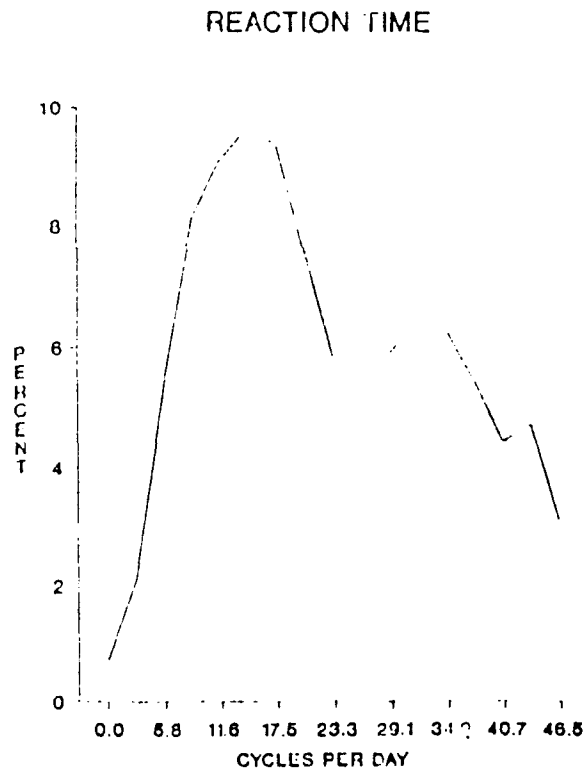


Figure 6 - Time series data for mean reaction time (Subjects 3 and 5)



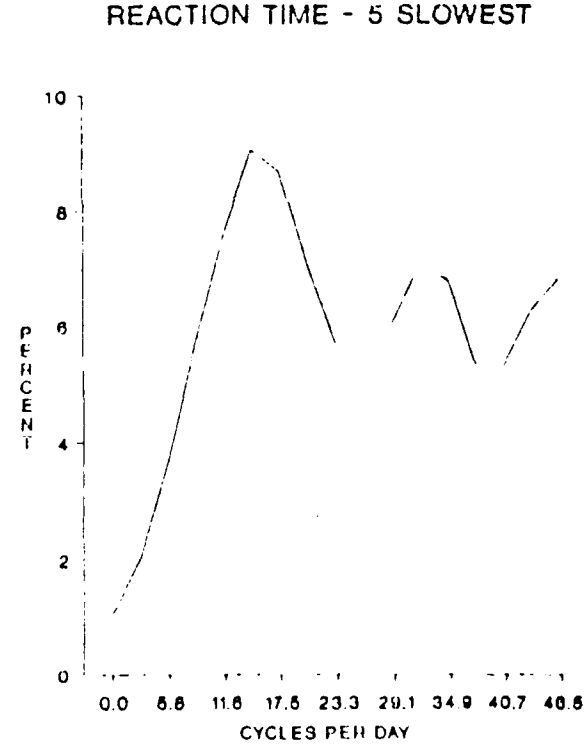


Figure 7 - Spectra for mean RT and Mean of the 5 slowest RTs (all subjects)

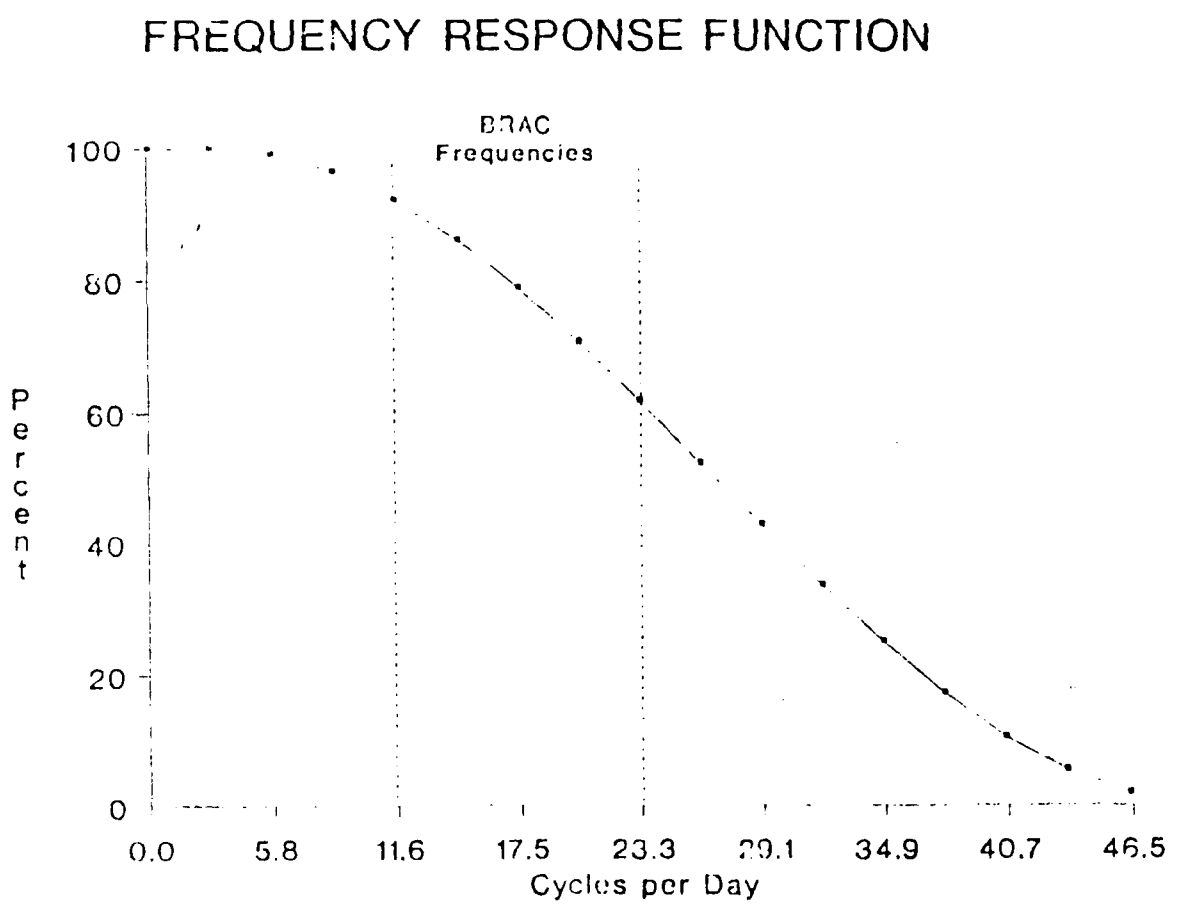


Figure 8 - Filter frequency response function

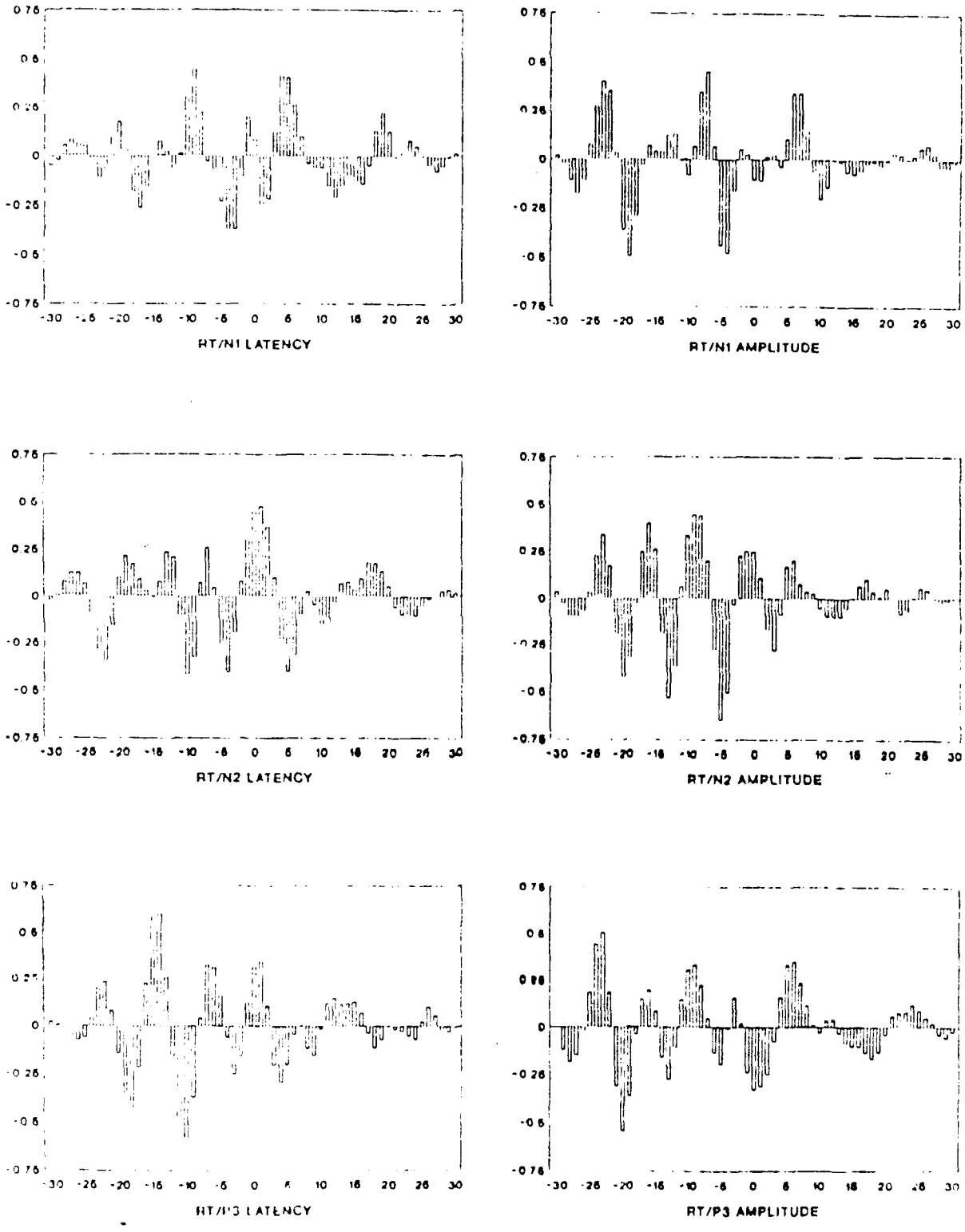


Figure 9 - Subject 1 ERP/RT Cross-correlation Functions

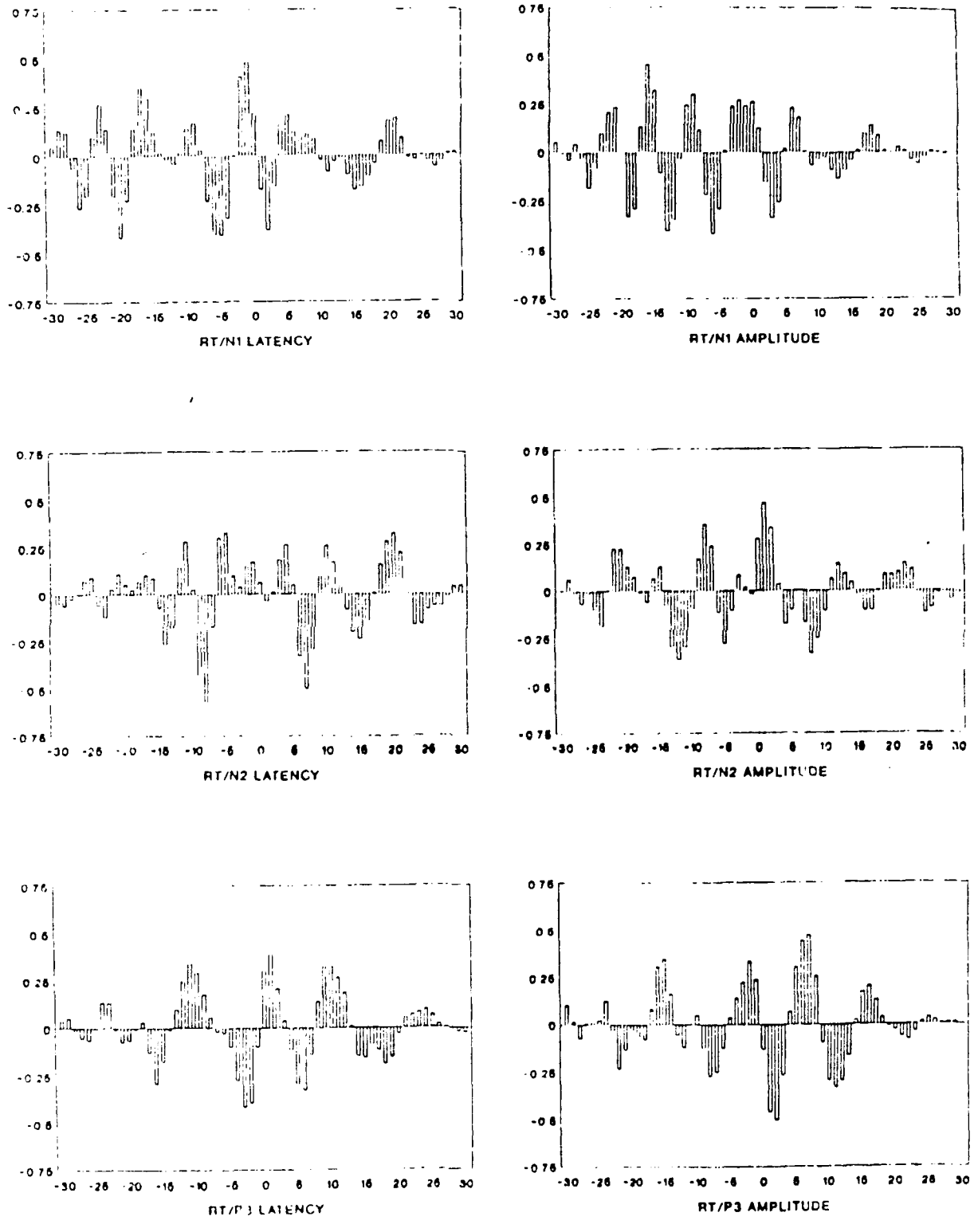


Figure 10 - Subject 2 ERP/RT Cross-correlation Functions

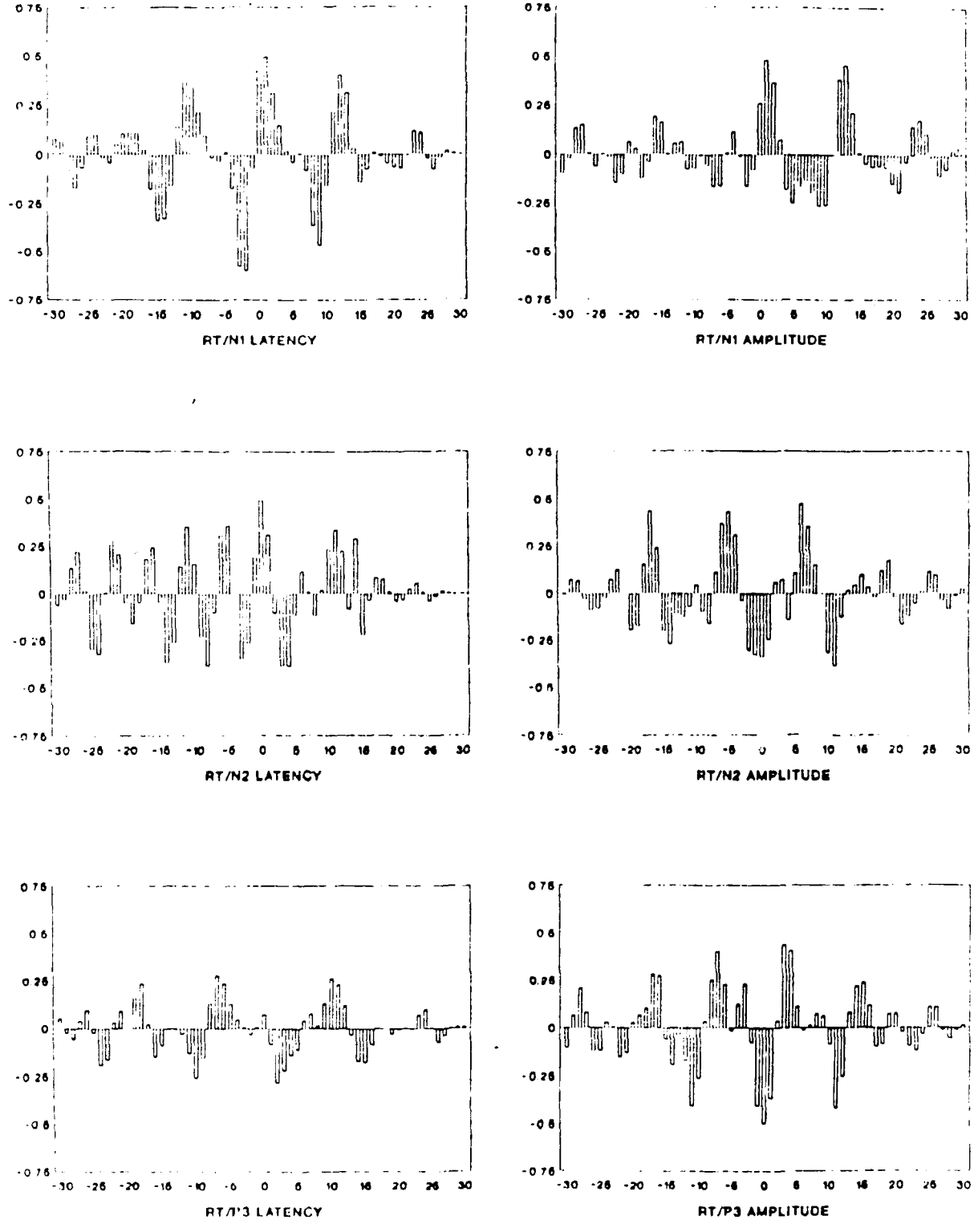


Figure 11 - Subject 3 ERP/RT Cross-correlation Functions

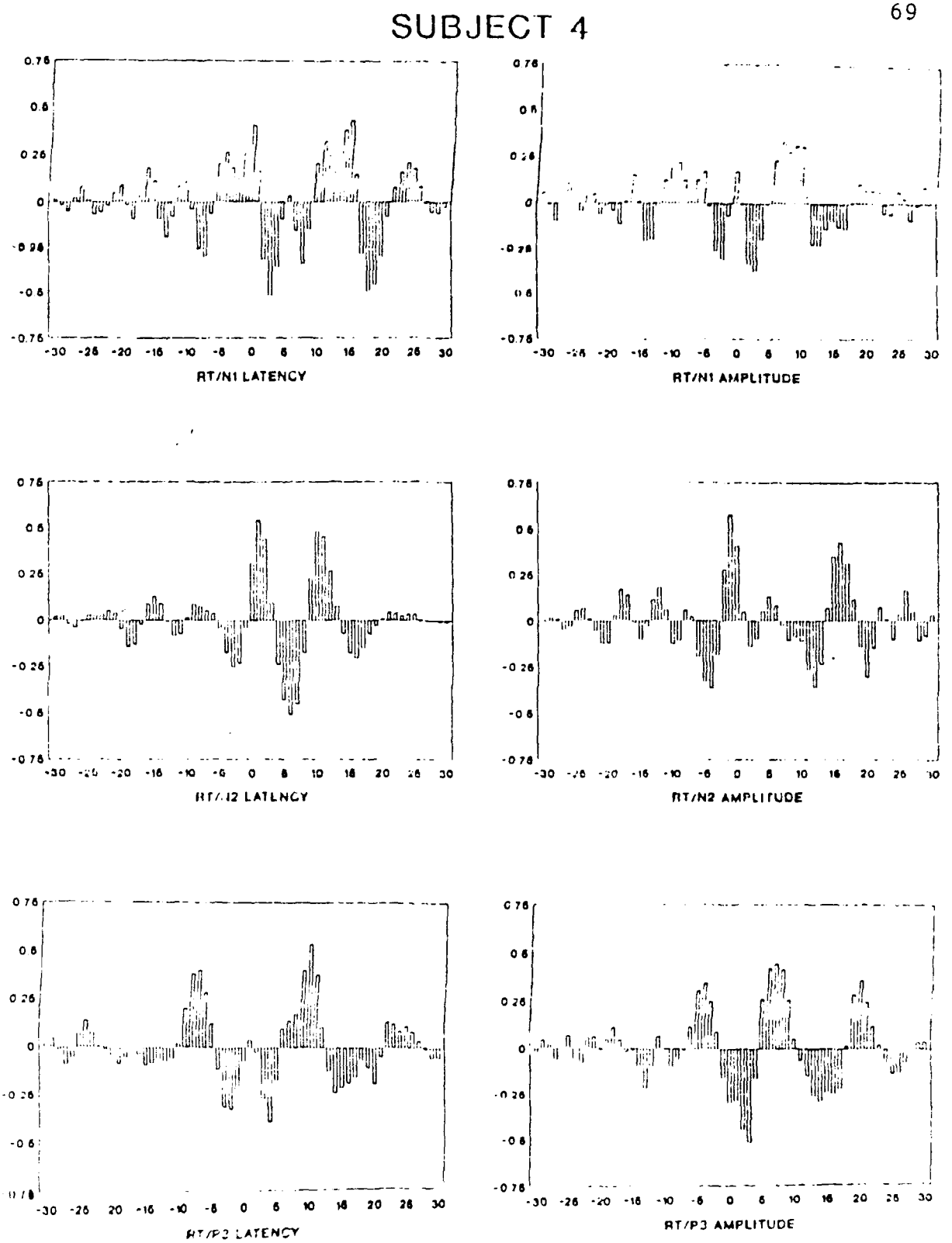


Figure 12 - Subject 4 ERP/RT Cross-correlation Functions

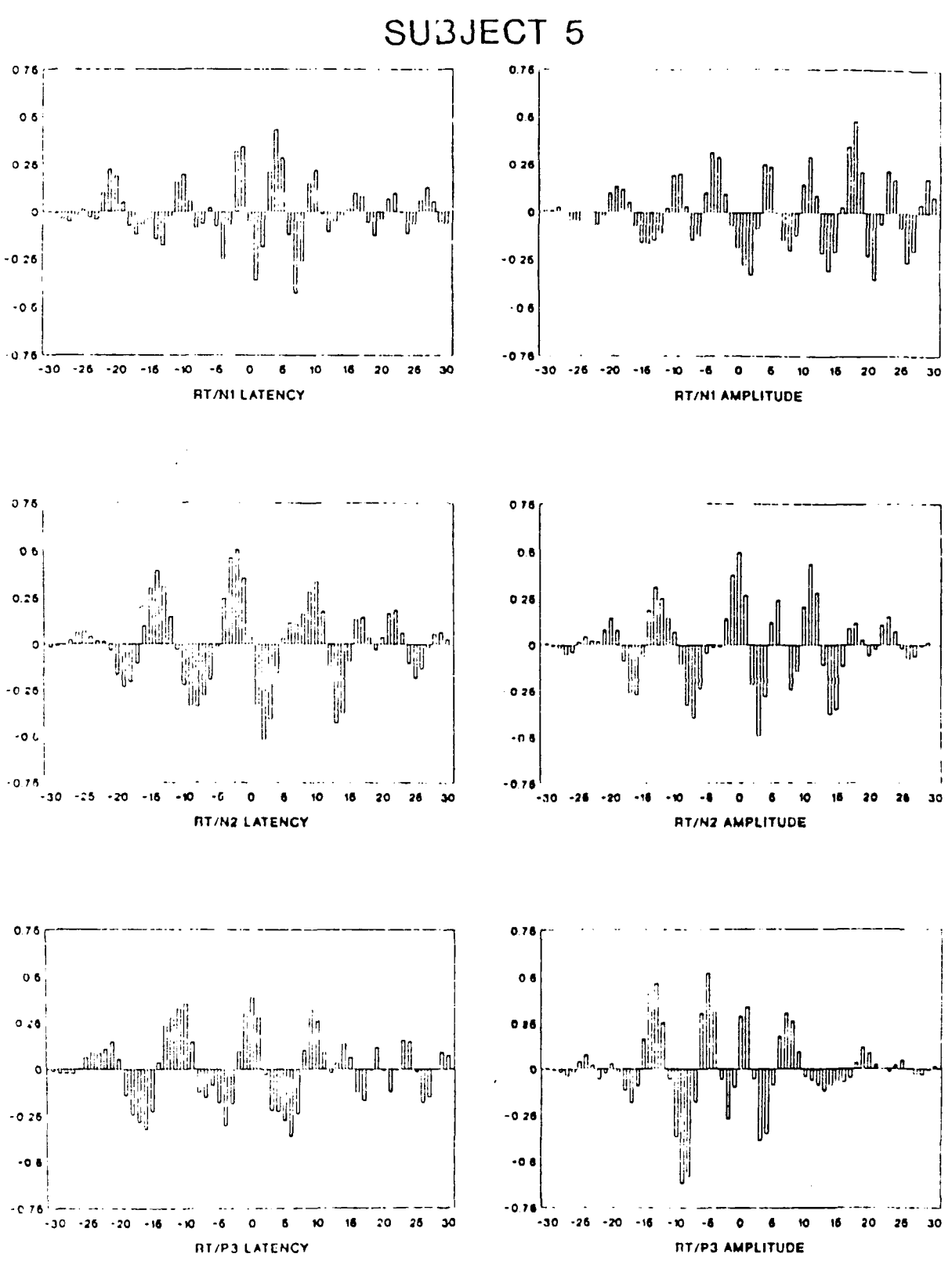


Figure 13 - Subject 5 ERP/RT Cross-correlation Functions

SUBJECT 6

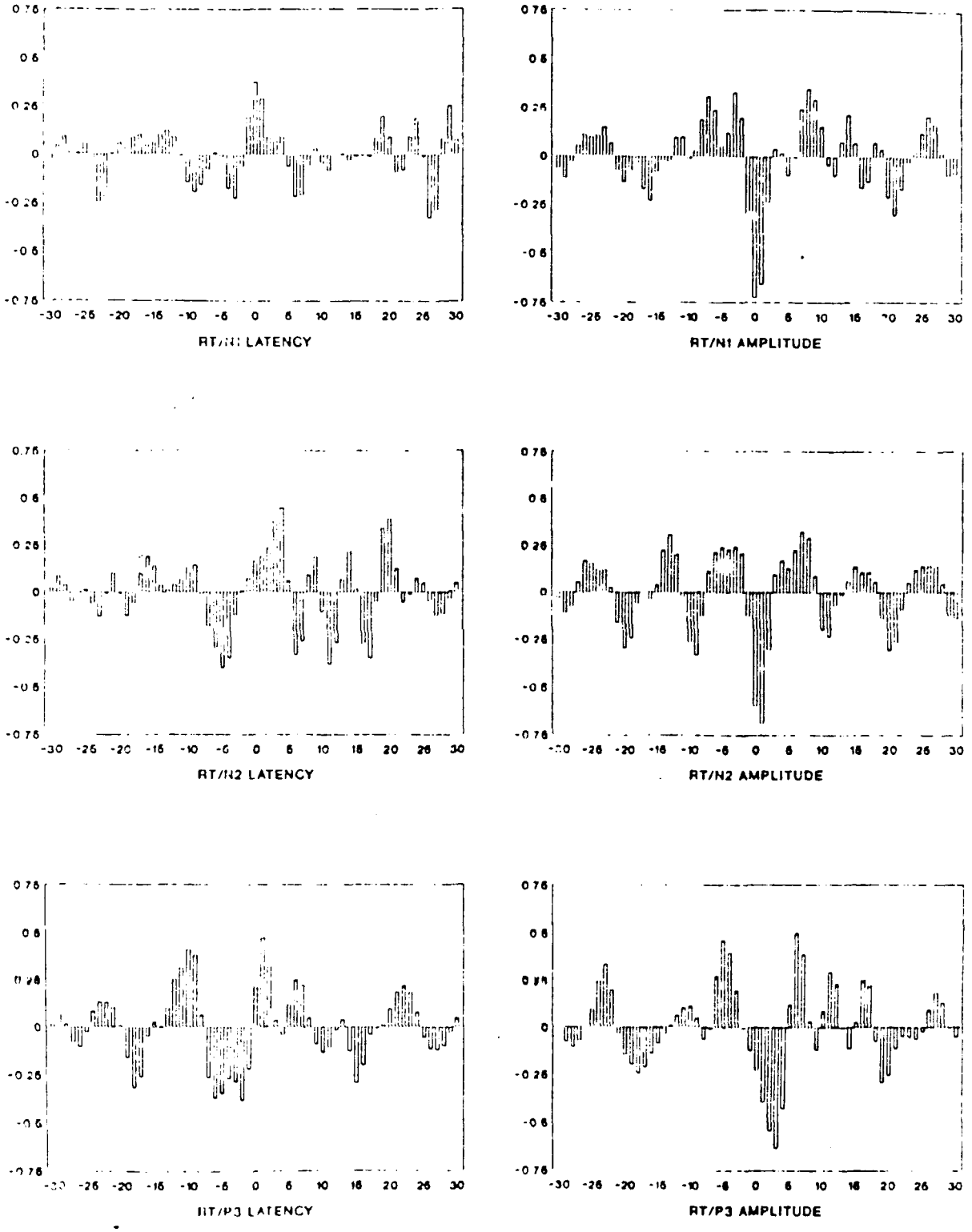


Figure 14 - Subject 6 ERP/RT Cross-correlation Functions

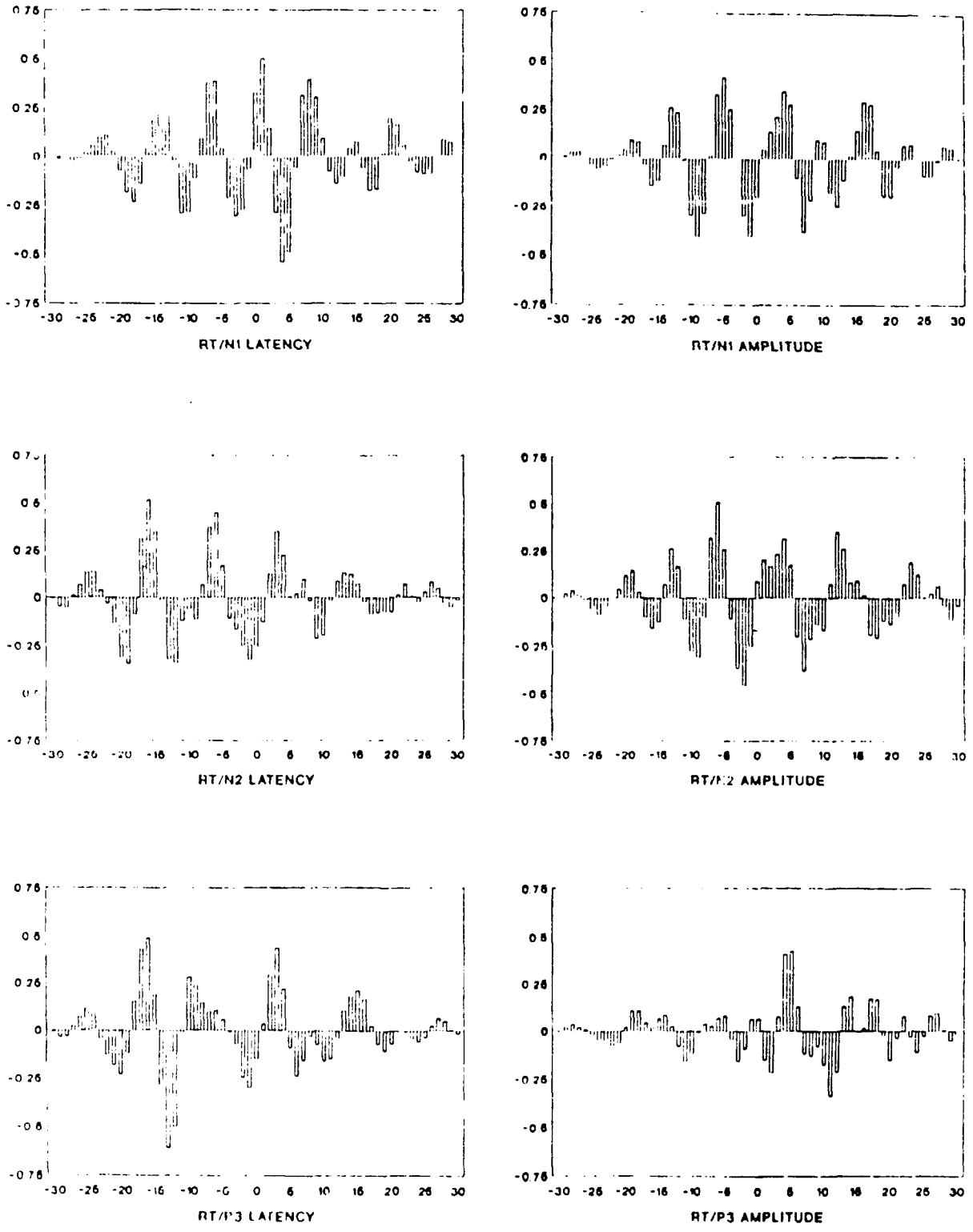


Figure 15 - Subject 7 ERP/RT Cross-correlation Functions

SUBJECT 8

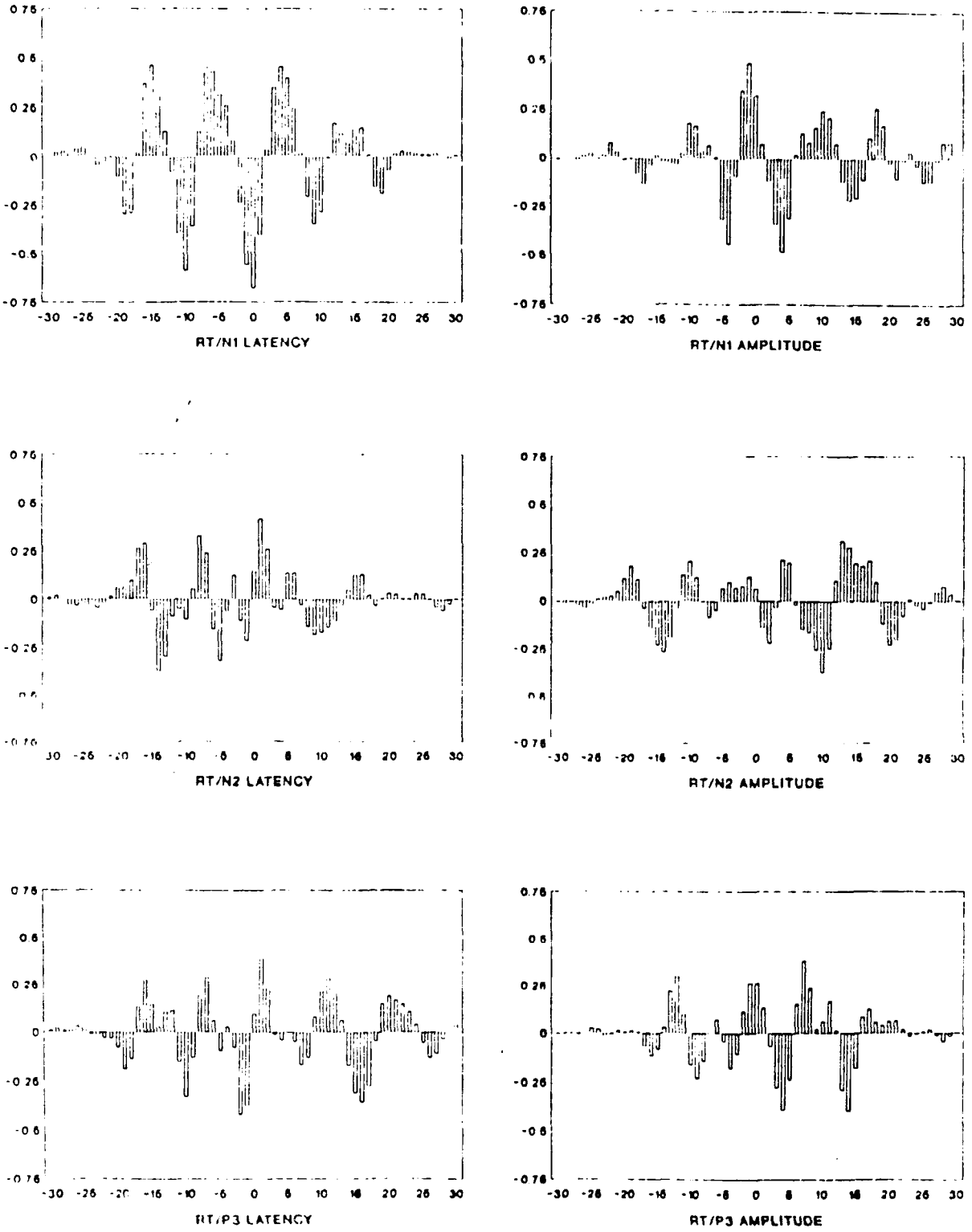


Figure 16 - Subject 8 ERP/RT Cross-correlation Functions

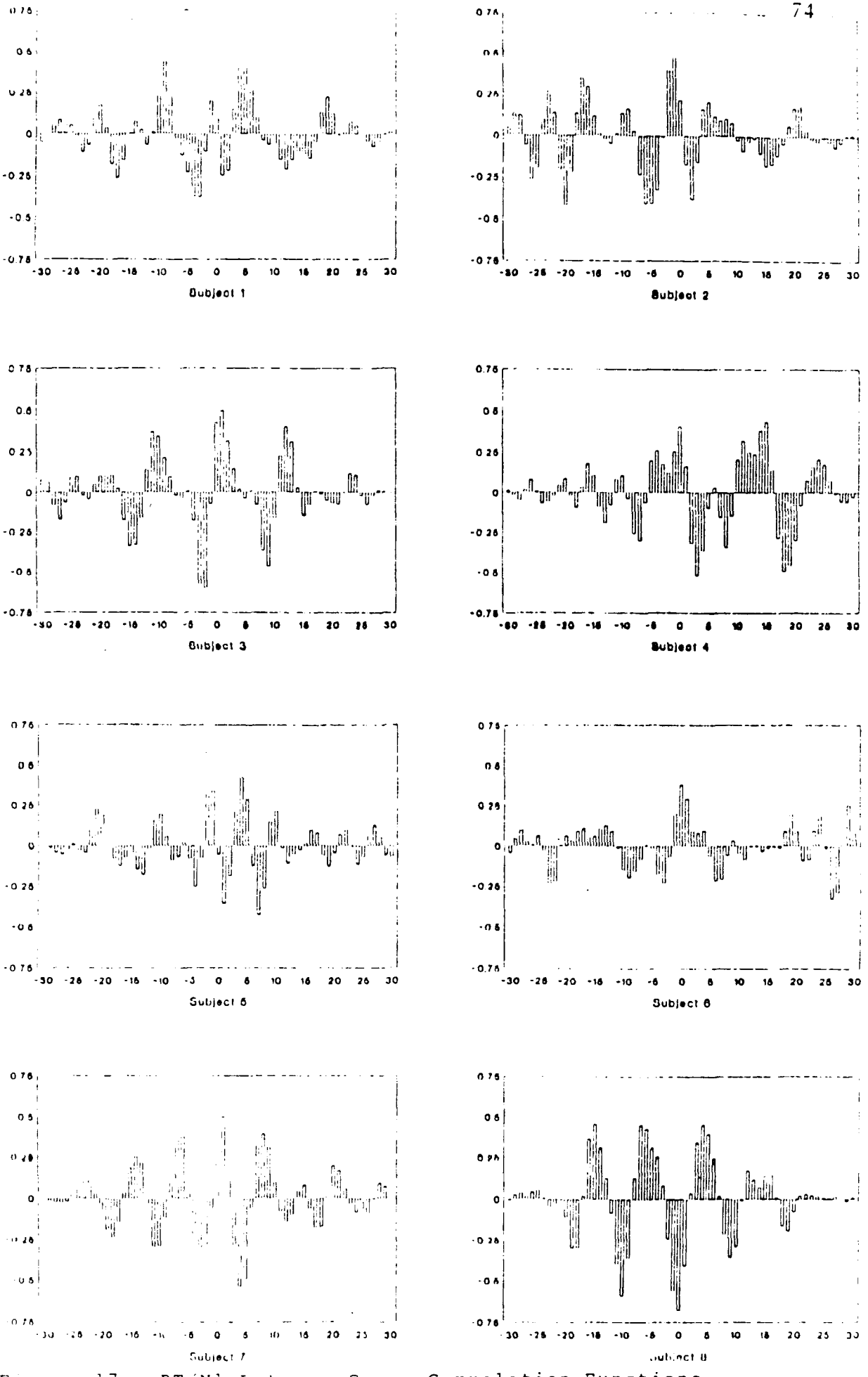
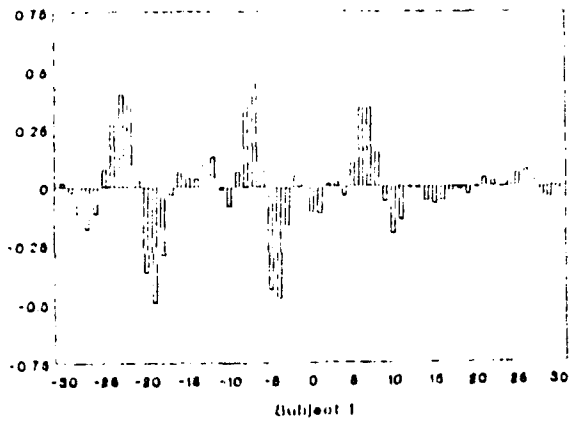
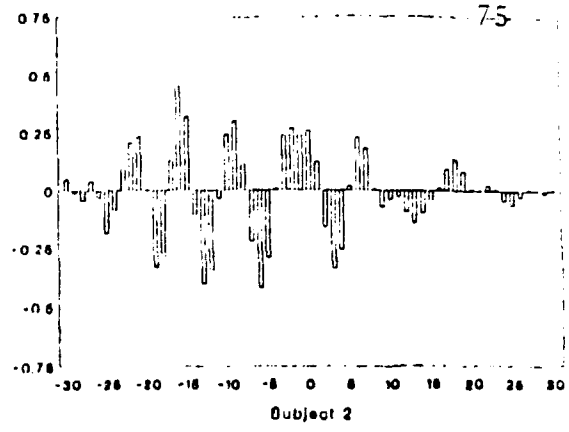
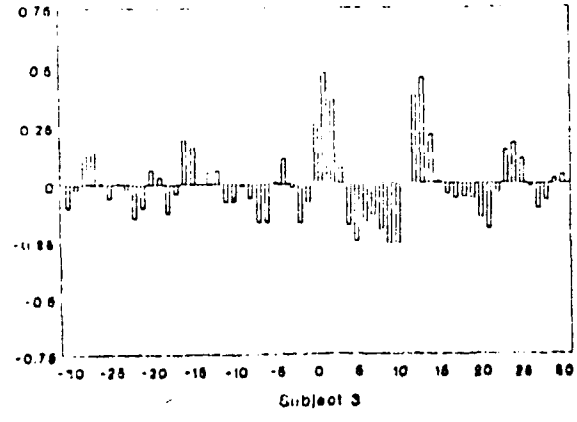
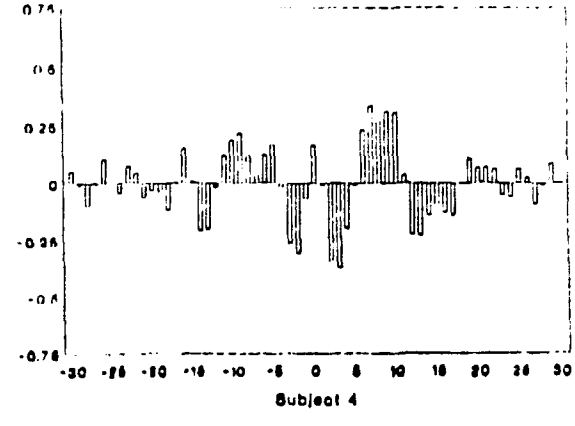


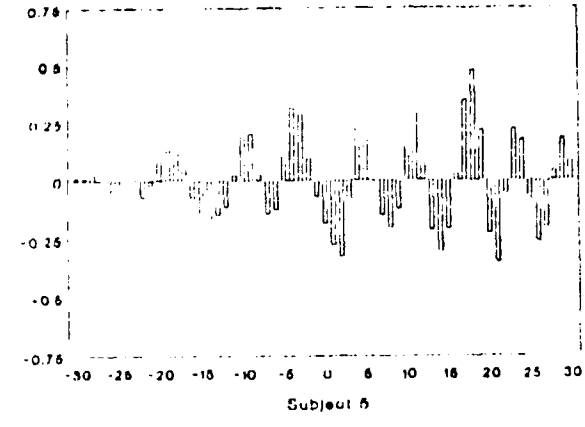
Figure 17 - RT/N1 Latency Cross-Correlation Functions

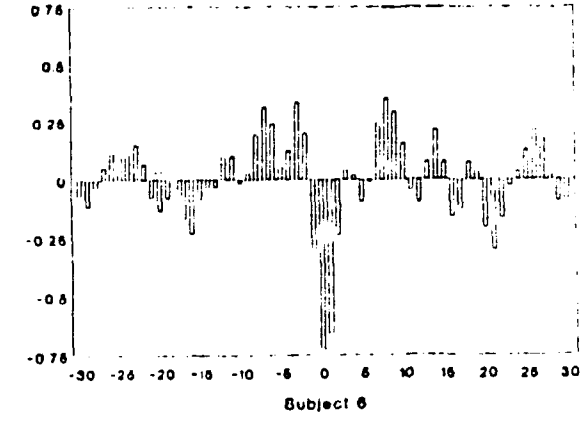


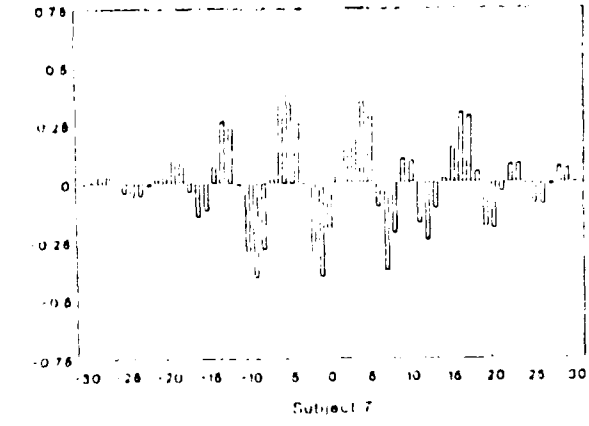












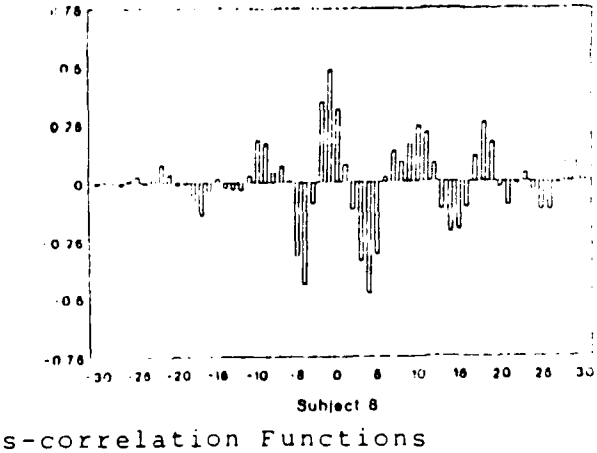
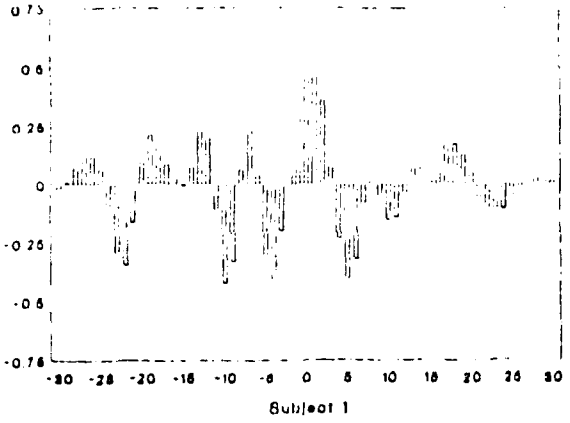
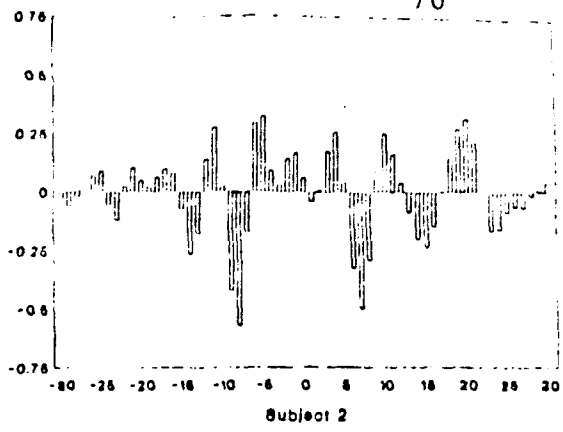
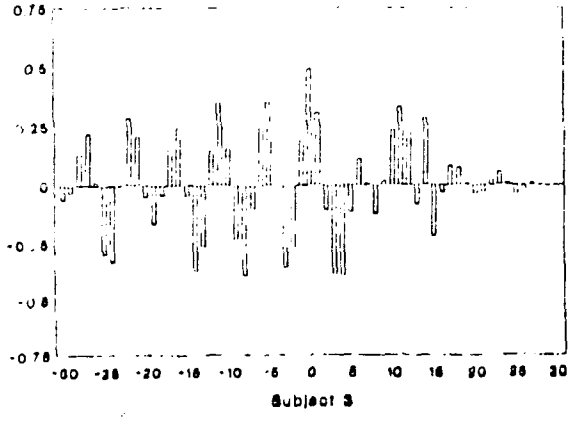
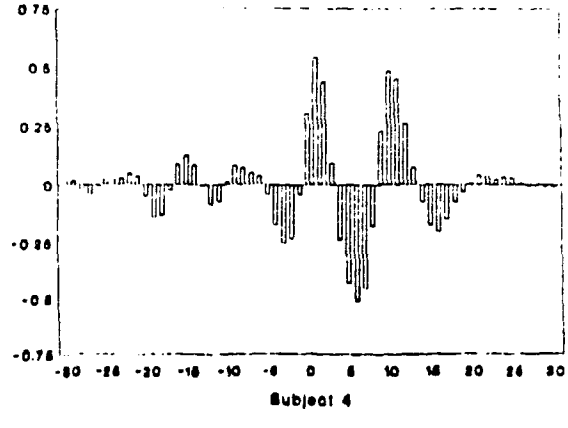


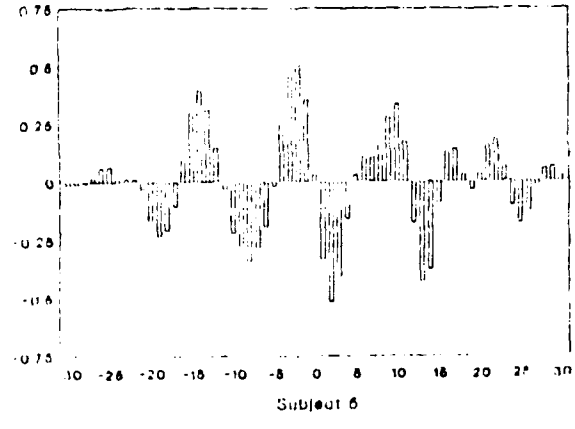
Figure 18 - RT/N1 Amplitude Cross-correlation Functions

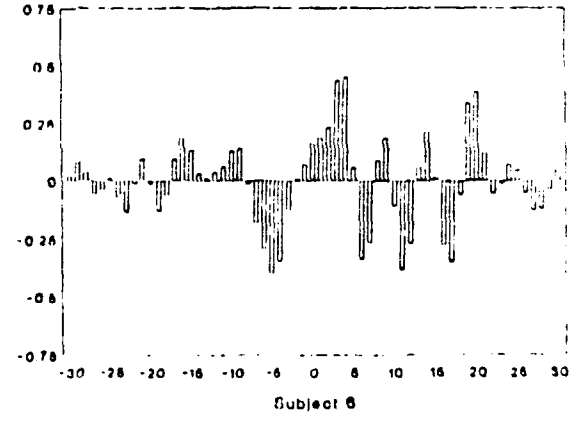


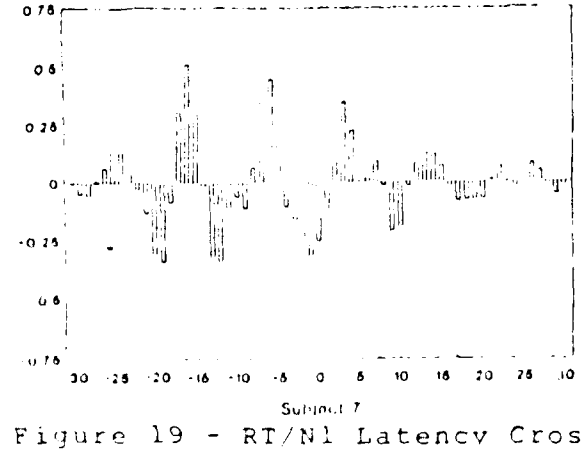












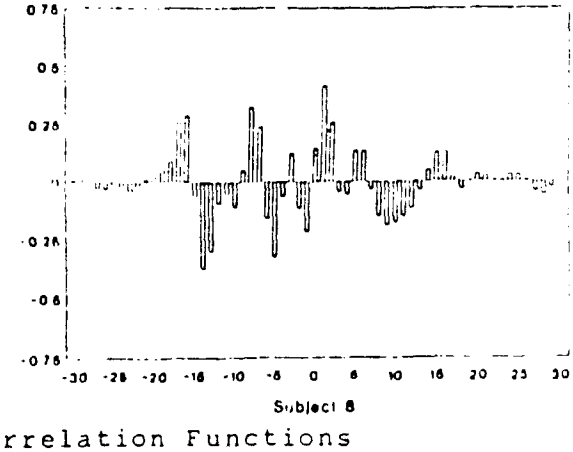


Figure 19 - RT/N1 Latency Cross-correlation Functions

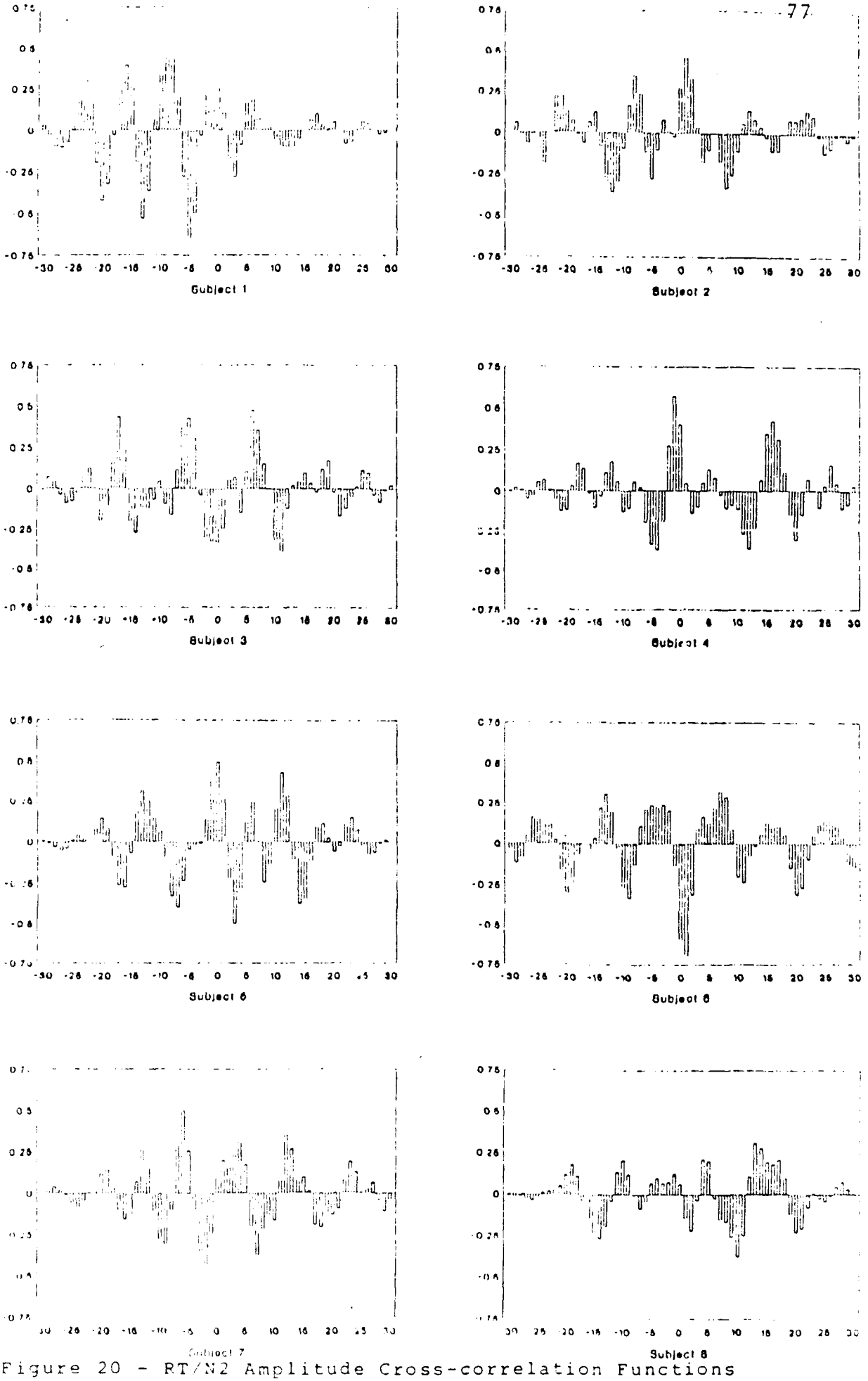
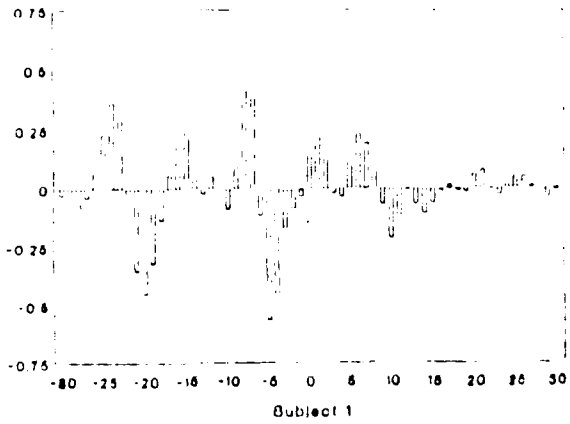
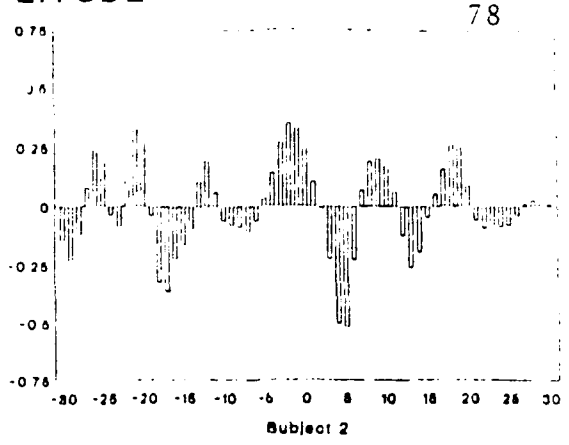
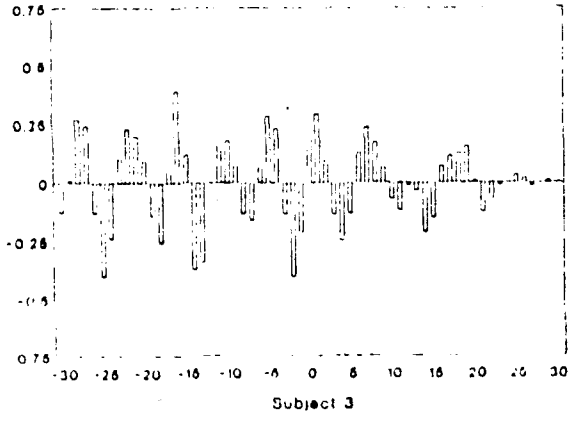
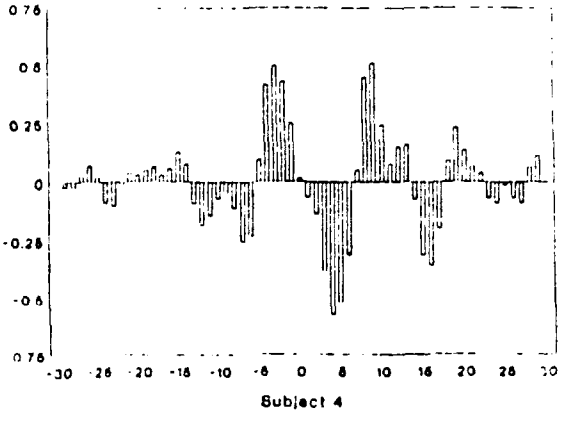


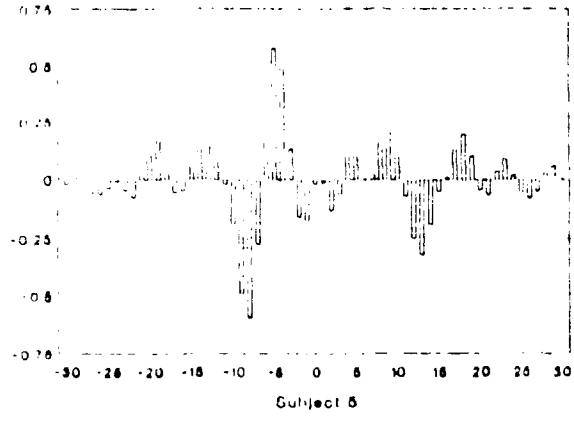
Figure 20 - RT/N2 Amplitude Cross-correlation Functions

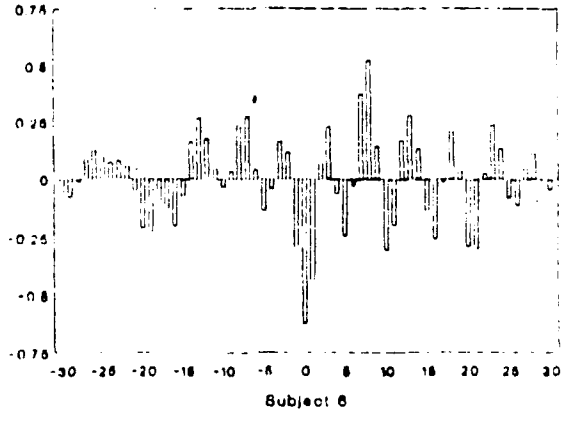


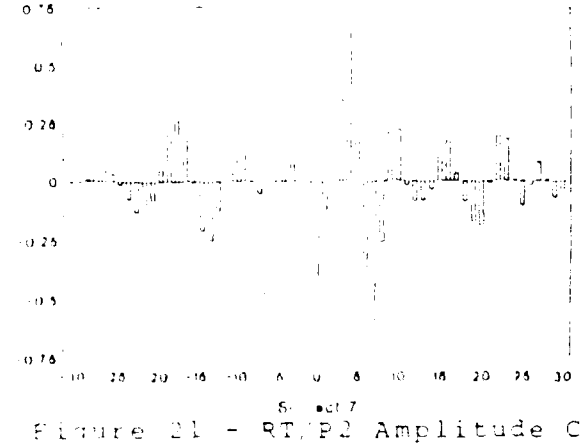












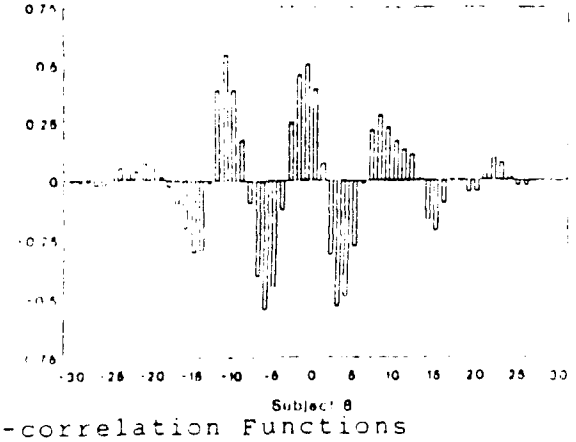
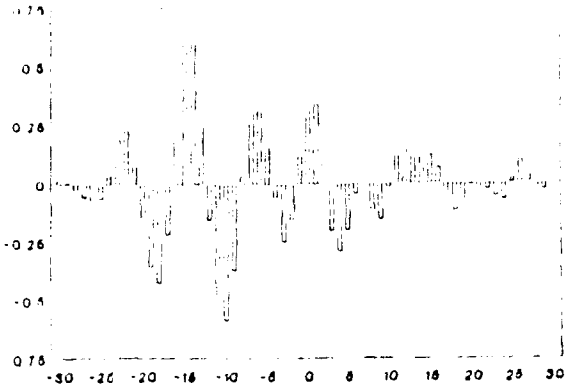
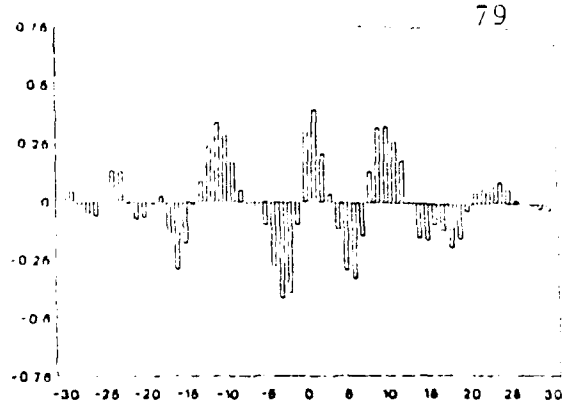
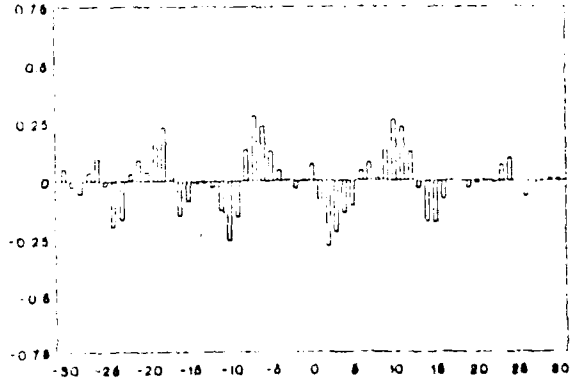
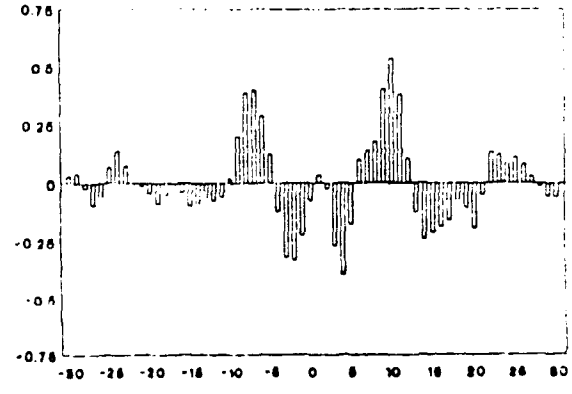


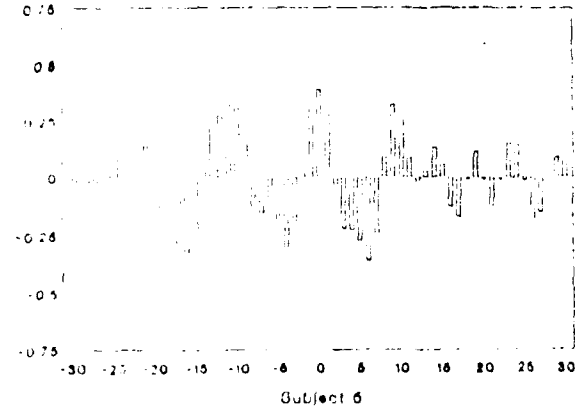
Figure 21 - RT/P2 Amplitude Cross-correlation Functions

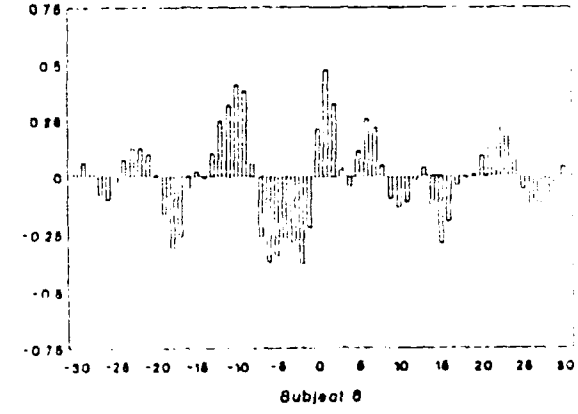


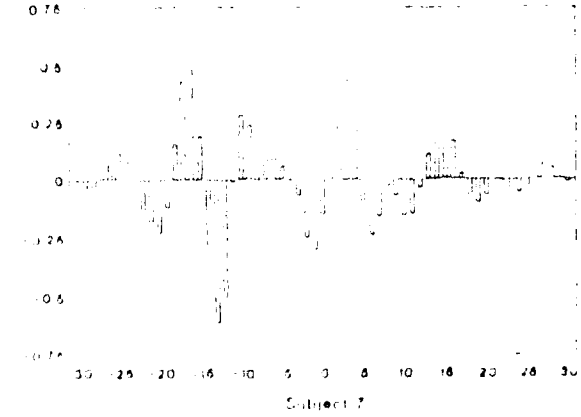












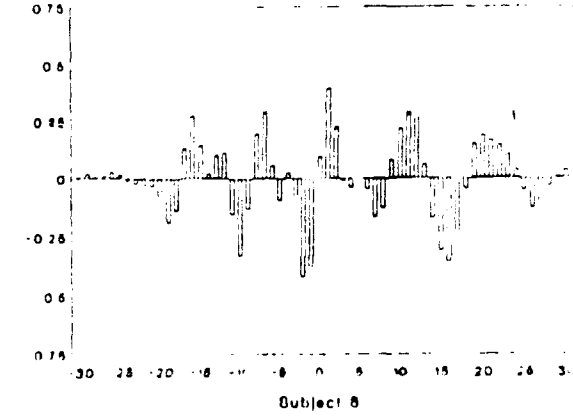


Figure 22 - RT/P3 Latency Cross-correlation Functions

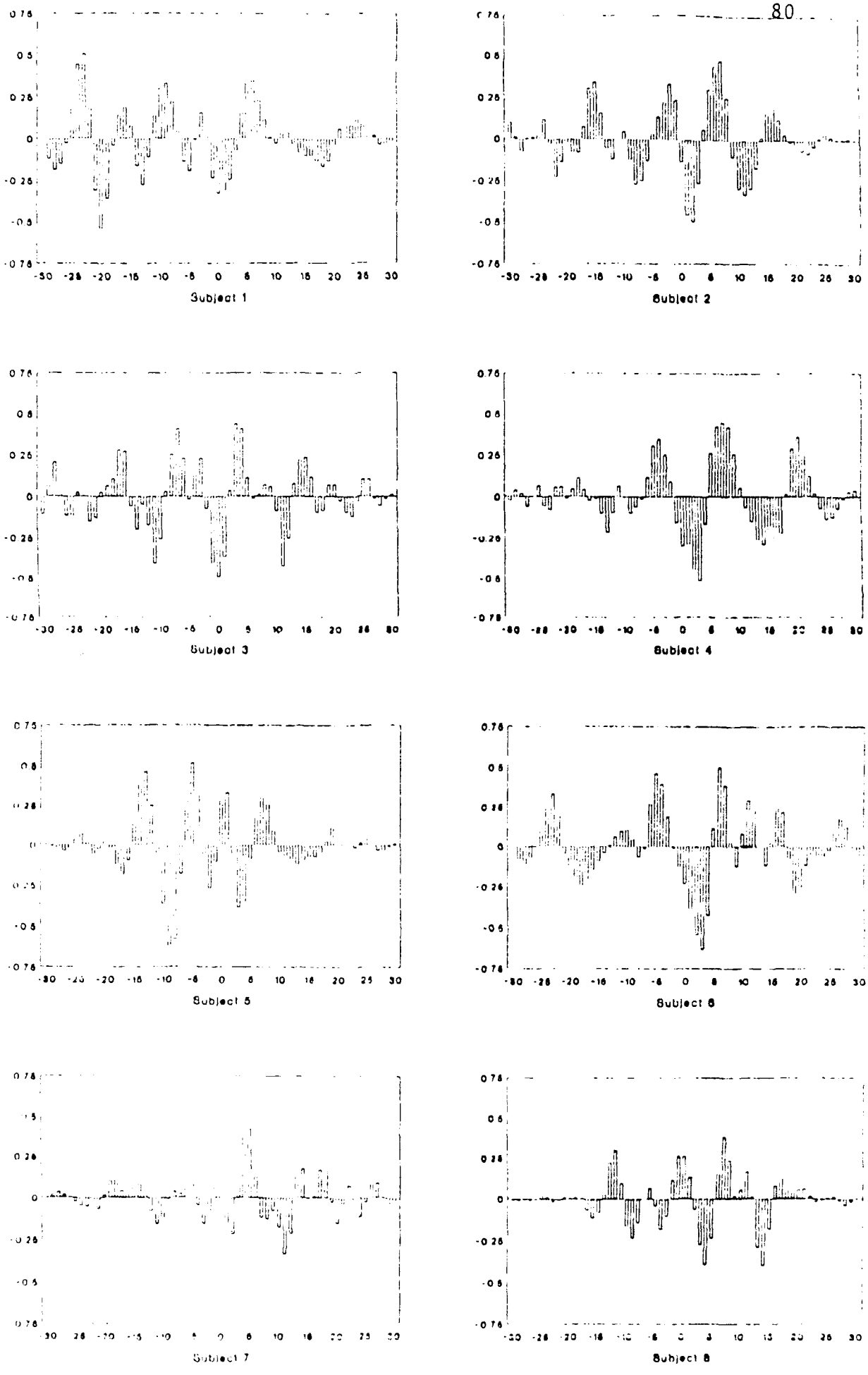


Figure 23 - RT/P3 Amplitude Cross-correlation Functions

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6.5 Experiment 5 - Repeated Testing, and Interblock Interval Effects on P300 Amplitude

Interest in the P300 since its discovery (Sutton, Braren, Ruben, & John, 1965) has been considerable. Factors affecting amplitude and latency of the P300 include, among others, task relevance (Roth, Ford, Lewis, & Kopell, 1976), stimulus probability (Duncan-Johnson & Donchin, 1977; Fitzgerald & Picton, 1981), and stimulus value (Begleiter, Porjesz, Chou, & Aunon, 1983). Such amplitude and latency effects suggest that P300 relates to changes in cognitive activities. The exact nature of these activities remains to be firmly established, but may include activities such as uncertainty resolution (Sutton et al., 1985), context-updating (Donchin, Ritter, & McCallum, 1978), and resource allocation (Kramer, Schneider, Fisk, & Donchin, 1986). However, the list of experimental manipulations affecting P300 amplitude and latency continues to grow (Johnson, 1986), suggesting that the pool of factors affecting P300 has not been exhausted.

One factor which has received only minimal attention when recording evoked potentials is time of day. Of those studies which have addressed time of day, conflicting results are reported. One study (Broughton, Aquirre, Dunham, & Suwalski, 1986) presented evidence of higher P300 amplitude at 1000 hrs than at 1400 hrs for normal subjects. Furthermore, amplitude measures taken across the day (1000, 1200, 1400, 1600 and 1800 hrs) displayed a sinusoidal pattern of change. For an age, sex, education and IQ-matched group of untreated narcolepsy-cataplexy patients, however, the reverse relationship held: amplitudes were slightly higher at 1400 hrs than at 1000 hrs. Other findings conflict with the above regarding time of day variations in normal subjects. Another P300 study (Kerkhof, 1980), using a signal-detection paradigm, reported that amplitude of the late positive component (LPC) displayed a diurnal variation; however, amplitude at 1000 hrs was significantly lower than amplitudes at 0400 hrs, 1600 hrs or 2200 hrs. This late positivity may have included other late positive slow-wave components as well as P300. Thus, it is still unclear whether a relationship between P300 and time of day exists. Research addressing the effects of time of day (i.e. , "circadian rhythms") on behavioral measures has shown that psychomotor (speed) measures tend to peak in the afternoon while measures of short-term memory (e.g. , digit span, free recall) tend to show a morning superiority (Blake, 1967; Folkard & Monk, 1980). The suggestion that behavioral measures peak at different times of day may have implications for research regarding cognitive factors indexed by evoked potentials. Given that P300 is thought to index higher cognitive capacities, it might be expected that a time of day variation in P300 would correspond with behavioral measures of the same underlying capacities.

A second variable which has recently drawn attention is the effect of repeated testing on amplitude of P300 to "target"

stimuli (Pritchard, Brandt, Shappell, Odell, & Barratt, 1986). That the P300 rapidly habituates to "nontarget" or "task-irrelevant" stimuli is well documented (Megela & Teyler, 1979). However, initial research led to the suggestion that P300 amplitude to targets was relatively resistant to change due to repeated testing (Donchin et al., 1984). Furthermore, most studies assessing "long-term" habituation of the P300 are of relatively short duration, i.e., less than one hour for a complete experimental session (Pritchard et al., 1986).

Conflicting findings have been reported regarding repeated testing. One study (Pritchard et al., 1986) assessed changes in P300 amplitude across a 3-hour experimental session and reported that P300 to both target and nontarget visual stimuli did not habituate. In contrast, another study (Parasuraman, 1983) reported that P300 amplitude to correctly detected targets declined across successive 10-minute blocks of a 30-minute auditory vigilance task. Amplitude decreased from approximately 10 uV (first 10 minutes of vigilance) to approximately 5 uV (last 10 minutes of vigilance). Although details of the latter study were not reported, one methodological difference between these two studies was the length of the interblock interval. The latter study (Parasuraman, 1983) tested continuously across 10-minute "blocks" (periods) of the vigilance task. In effect, no interblock interval was used. Conversely, the former study (Pritchard et al., 1986) allowed subjects a 2-minute rest interval between 10-minute blocks. This extended interblock interval may have resulted in dishabituation of P300 between blocks.

The present study addressed three questions. The first question addressed whether time of day factors affected P300 amplitude. A second question concerned whether amplitude of the P300 to target stimuli would show a decrement (habituate) with repeated testing, and whether this factor interacted with time of day. Our final question addressed whether the pattern of change in P300 amplitude due to repeated testing would be altered by extending the interblock interval between one pair of test blocks.

Method

Subjects Fifty normal, healthy undergraduate students (32 females, 18 males) enrolled in Psychology 201 courses participated in the experiment. All were screened for hearing, health/sleep problems, and medication use (e.g. , stimulants). They were told to obtain a normal night's sleep prior to participation and to refrain from alcohol and caffeine the day of the experiment.

Apparatus A Grass Model 7P122 DC amplifier (time constant = .1 seconds, half-pass filter = 35 Hz, 60 Hz notch filter out) was used to record and filter the auditory evoked potential (AEP). Averaging was controlled by Computerscope Hardware/Software driven by an Apple IIe microcomputer. Tone stimuli (rise time = 4 ms) were controlled by a Commodore 64 microcomputer. Grass Model 7P211 AC amplifiers were used to record

electroencephalographic (EEG), electrooculogram (EOG) and electromyogram (EMG) signals during daytime naps. All signals were recorded using Grass silver/silver chloride electrodes filled with Grass EC2 electrode cream.

Procedure Subjects were instructed to arrive at the Psychophysiology Laboratory at 0800 hrs for morning sessions or 1400 hrs for the afternoon sessions. They were given a brief description of the procedure upon arrival and an informed-consent sheet to sign. Next, areas for EOG (outer canthi, above and below midline) and EMG (mental-submental) were cleaned, abraded, and electrodes applied with tape. Areas for EEG (Cz, Oz, left and right mastoids) were cleaned, abraded, and electrodes secured with collodion. Impedance was kept below 5 K ohms for all electrode sites. Subjects then were seated in a recliner and given instructions to count high-pitched (target) tones and to make a brief finger-lift response to each target tone. They then put on headphones and several low and high pitched tones were presented. Both low and high-pitched tones were 500 ms duration, 65 dB SPL against an ambient room background of 55 dB, and were presented binaurally through the headphones. Probability of the high-pitched target tones was .2 and the low-pitched nontarget tones was .8. Subjects were told to keep their eyes closed and to avoid sudden body movements during stimulus presentations. The experimenter monitored the subjects continuously during stimulus presentations to ensure that a finger-lift response occurred for every target presentation. Subjects who failed to respond on every occasion were eliminated from statistical analyses. Target and nontarget tones were presented in a random order with a fixed 1500 ms interval (tone onset to tone onset). The number of targets presented for each block varied from 35 to 45 so that subjects could not determine the number of tones presented without counting. The first 35 artifact-free targets were averaged. Evoked potentials contaminated by excessive eye or muscle artifact were rejected on-line by the Computerscope. The EEG was sampled from the Cz placement for 100 ms prior to stimulus onset and for an additional 710 ms following stimulus onset at a rate of one sample every 3.96 ms. At the end of each block, subjects reported how many target tones they counted.

From each of the morning (n = 25) and afternoon (n = 25) groups, 10 subjects were randomly assigned to a one-hour "awake" condition and 10 were assigned to a one-hour "nap" condition (see Footnote 1). The remaining 10 subjects (5 morning, 5 afternoon) were assigned to a "control" condition. All subjects (n = 50) were tested across six blocks. The interval (interblock interval) between Blocks 1 and 2 and between Blocks 3, 4, 5 and 6 was 30 seconds for all conditions (awake, nap and control). However, the interval between Blocks 2 and 3 was different for the awake and nap conditions versus the control condition. The interval between Blocks 2 and 3 was one hour for subjects in the awake and nap conditions (subjects in the latter condition were allowed to nap during this time) and 30 seconds for subjects in the control ("equal interblock interval") condition.

Results Amplitude of P300 was measured as the difference between baseline averaged over the 100 ms prestimulus period and peak of the most positive-going component occurring approximately 300 ms subsequent to stimulus onset (mean P300 latency = 327.98 ms). Figure 1 illustrates P300 amplitude across test Blocks 1 - 6 for morning versus afternoon groups (collapsed across Nap, Awake, and Control conditions). As seen in Figure 1, amplitude of P300 demonstrated a marked time of day effect. Overall amplitudes were higher in the morning compared to afternoon across all blocks. The difference between morning and afternoon sessions was confirmed statistically (Time of Day main effect, $F[1, 44] = 6.00$, $p < .05$). Although the pattern of amplitude decrement across blocks appeared to differ for morning versus afternoon sessions, the Time of Day x Block interaction was not significant.

Repeated testing Figure 2 displays P300 amplitude across blocks for subjects in the awake, nap, and control conditions (collapsed across Time of Day). As evident from Figure 2, amplitude of P300 decreased slightly from Block 1 to 2 for the awake and nap conditions but increased slightly for the control condition. Amplitude increased from Block 2 to 3 for both the awake and nap conditions (one-hour interval) but showed a sharp decrease for the control condition (30-second interval). Amplitude decreased across the next three blocks for all three conditions. The decrease from Block 3 to 4 appeared to be greater for the awake and nap conditions than for the control condition. A graphic illustration of the decrement in P300 amplitude across the experimental session can be seen in Figure 3. This figure represents the averaged waveform for Block 1 (mean) vs. Block 6 (mean), collapsed across Time of Day and Condition factors. As seen in Figure 2, a decrement in P300 amplitude occurred from Block 1 to Block 6. Also evident from Figure 2 is that the decrement in P300 was due to a diminution in the overall area of P300 as opposed to a redistribution of the area of the curve. A significant Block main effect was found ($F[5, 220] = 18.94$, $p < .05$). Post-hoc Tukey HSD performed on mean P300 amplitude for Blocks 1 through 6 revealed that amplitude at Block 6 was lower than Blocks 1 through 4 ($q[6, 220] = 1.69$) and amplitude at Blocks 4 and 5 were lower than Blocks 1, 2 and 3. Blocks 1, 2, and 3 did not differ nor did Blocks 4 and 5 or Blocks 5 and 6.

Interblock interval As noted above and in Figure 2, the awake and nap conditions demonstrated an increase in P300 amplitude across the extended interval from Block 2 to 3. The increase from Block 2 to 3 was higher for the awake condition (mean increase of 1.09 uV) than for the nap condition (mean increase of .49 uV). The control condition (30-second interval), however, demonstrated a marked decrease in amplitude ($x = 3.73$ uV) from Block 2 to 3. An ANOVA performed on P300 amplitude (Blocks 2 to 3 only) revealed a significant Condition x Block interaction, $F[2, 44] = 5.31$, $p < .05$), confirming these observations. Further one-way analyses comparing P300 amplitude

from Block 2 to 3 separately for each condition revealed that while the amplitude decrement from Block 2 to 3 was significant for the control group, $F(1, 9) = 8.95$, $p < .05$, the amplitude increase from Block 2 to 3 for the nap and awake groups was not significant ($p > .05$). No further main effects or interactions were significant.

Discussion Amplitude of P300 clearly was affected by time of day. These effects are consistent with prior research (Broughton et al., 1986) assessing amplitude changes in normal subjects across the day (i.e., higher P300 amplitudes in the morning than in the afternoon). That time of day impacts on P300 amplitude is important in that it may reflect cognitive processes whose behavioral measures vary in the same direction. This time of day effect for P300 amplitude in fact parallels variations in behavioral tasks involving memory capacities such as speed of learning noted as early as 1885 by Ebbinghaus (Woodworth & Schlossberg, 1956), and more recently for tasks of immediate memory such as digit span (Blake, 1967) and of short-term memory such as free P300 recall (Folkard & Monk, 1980), i.e. , better performance in the morning than in the afternoon. Moreover, the decrement in P300 amplitude noted for the afternoon condition may coincide with the decrement noted for behavioral measures. That is, the first test block of the afternoon condition in the present study (approximately 1430 hrs) occurred within a time frame previously demonstrated to correspond with a temporary decrease in performance between 1300 and 1500 hrs (Blake, 1967; Colquhoun, 1971). Thus, it is possible that changes in both performance (Blake. 1967) and P300 amplitude (Broughton, 1986; present study) reflect changes in cognitive capacities. Although only two test points were assessed within a 24-hour period in the present study, the direction of P300 amplitude change is consistent with others (Broughton et al. 1986) and warrants further investigation of variations in P300 amplitude across 24 hours.

Repeated Testing and Interblock Interval Effects Amplitude of P300 clearly showed habituation with repeated testing. The rate of habituation, however, was altered by inserting a one-hour interval between blocks. Whether the interval consisted of sleep or wakefulness was not an important factor, as both wake and nap conditions demonstrated a slight increase in amplitude from Block 2 to 3. Thus, P300 amplitude is affected by both repeated testing and the interblock interval. The P300 habituation across blocks noted in the present study may have been related to the interstimulus interval. Others have demonstrated that interstimulus intervals affect P300 amplitude. For example, prior research [10] has demonstrated that P300 amplitude was lower at shorter interstimulus intervals (higher temporal probability), regardless of sequential probability. However, that study (Fitzgerald & Picton, 1981) did not determine the effects of interstimulus intervals across repeated testing (i.e., habituation). The present results suggest that any effects due to short interstimulus intervals (Fitzgerald & Picton, 1981) can be

attenuated by the length of the interblock interval. In effect, inserting a long interblock interval eliminated habituation on the subsequent block. Another study (Pritchard et al., 1986) also reported no decrement in P300 amplitude to target stimuli with long (2 minutes) interblock intervals. Thus, both interstimulus and interblock intervals can affect the P300 component.

The finding that P300 amplitude decreases with repeated testing also may relate to the allocation of resources for the detection and counting task (Israel, Chesney, Wickens, & Donchin, 1980). That is, due to perceived experimental demands, etc., subjects may have "over-allocated" resources to the task during the initial test blocks. This allocation is reflected in high amplitude P300. However, because the task is relatively easy, with continued testing subjects learn to allocate fewer resources to the task (P300 decreases) while continuing to perform accurately. Although the present study did not directly assess "resource allocation" by invoking a concurrent task (Israel, Chesney, Wickens, & Donchin, 1980; Schneider & Fisk, 1982), subjects did report engaging in other mental activities (e.g. , daydreaming) while performing the task. Others have reported that P300 amplitude to counted tones decreases when the counting task is made secondary although counting accuracies themselves are not affected significantly (Israel et al., 1980). It is unlikely that methodological factors contributed to P300 habituation. One might argue that the use of a short time constant (.1 seconds) affected P300 amplitude. In effect, P300 amplitude is lower at shorter time constants (Duncan-Johnson & Donchin, 1979). However, since the time constant was not altered across blocks, any effect of attenuation on P300 amplitude would be constant across all blocks. More important, P300 habituation with repeated testing also has been demonstrated using a longer (.8 seconds) time constant (Lammers & Badia, 1991) and the difference in P300 amplitude between a time constant of .8 seconds and much longer ones (e.g., 10 seconds) is minimal. Second, the long stimulus duration (500 ms) may have affected P300. However, P300 amplitude decrements have been replicated both at this stimulus duration [16] and at shorter (50 ms) stimulus durations (Lammers, Wesensten & Badia, 1987). Finally, although changes in P300 component structure was not assessed via multiple site (scalp distribution) measures, similar P300 habituation effects with repeated testing have been recorded at both the parietal (Pz) and frontal (Fz) scale sites (Lammers & Badia, 1991).

In sum, the present study indicates that the processes indexed by P300 are affected by time of day, repeated testing, and interblock intervals. Time of day effects suggest a circadian variation in cognitive processes underlying P300, while repeated testing and interblock interval effects suggest changes in the allocation of these processes with time on task.

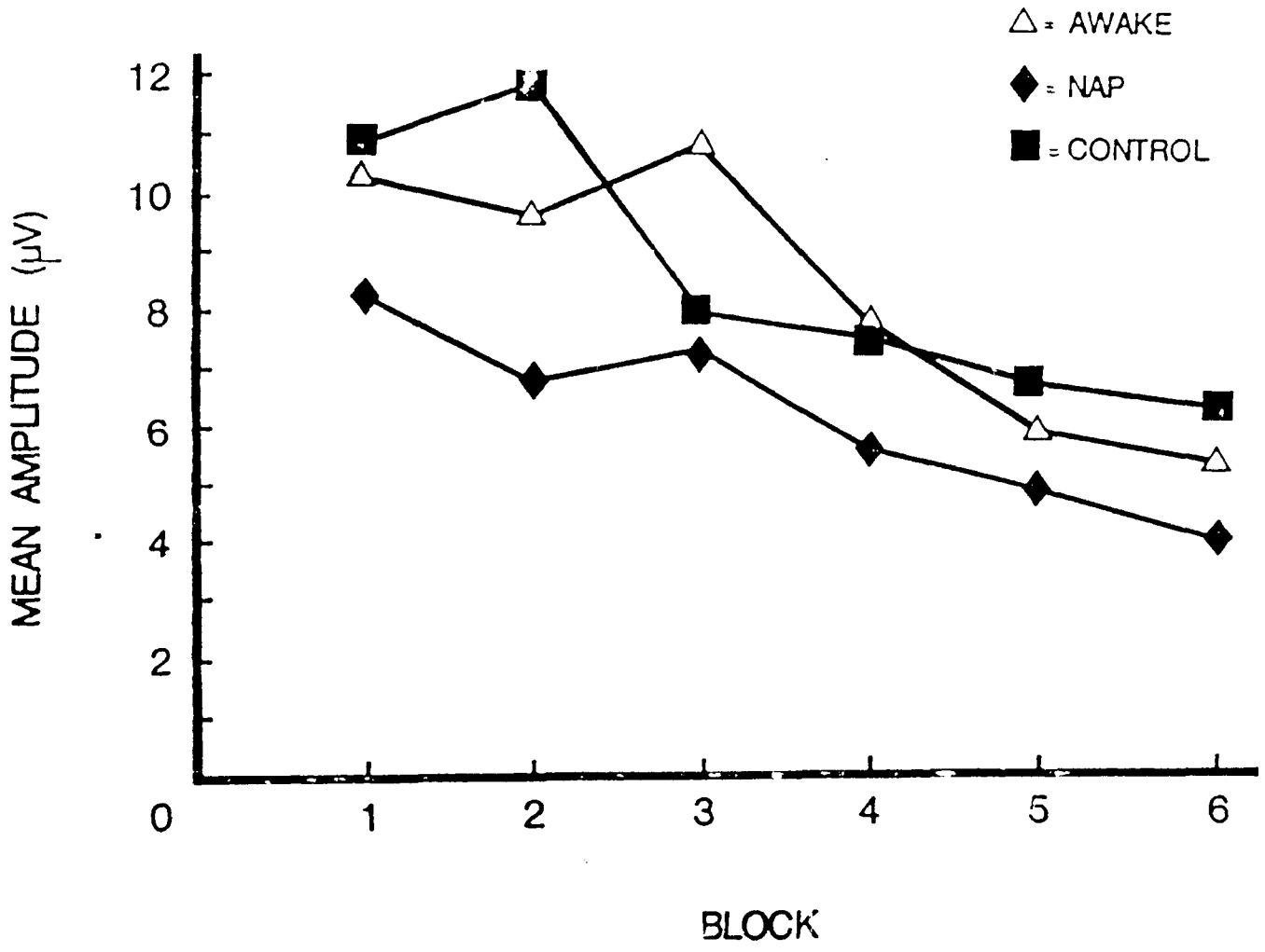

Figure 1. P300 amplitude across blocks for morning versus afternoon sessions.

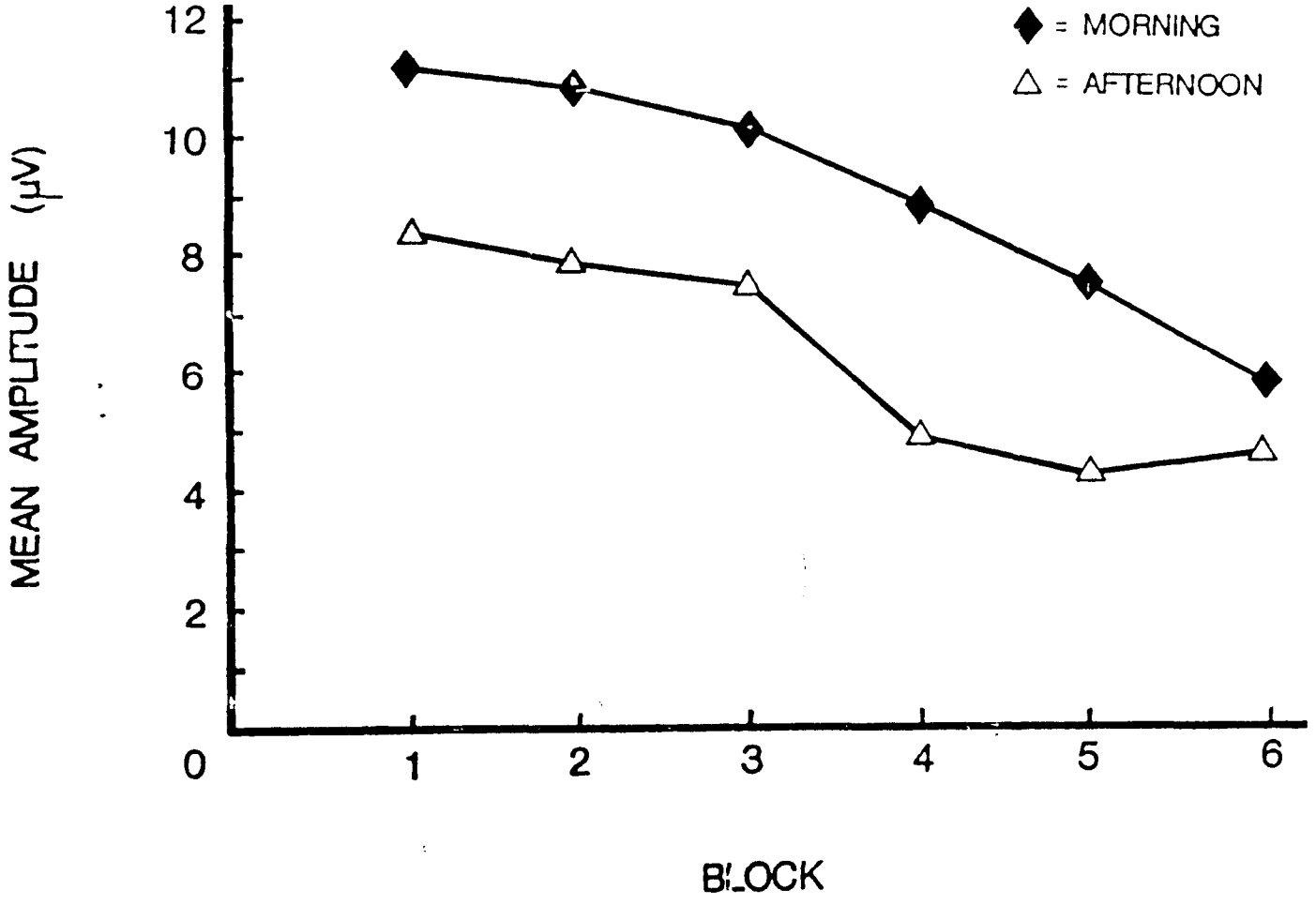

Figure 2. P300 amplitude across blocks for awake, nap and control conditions.

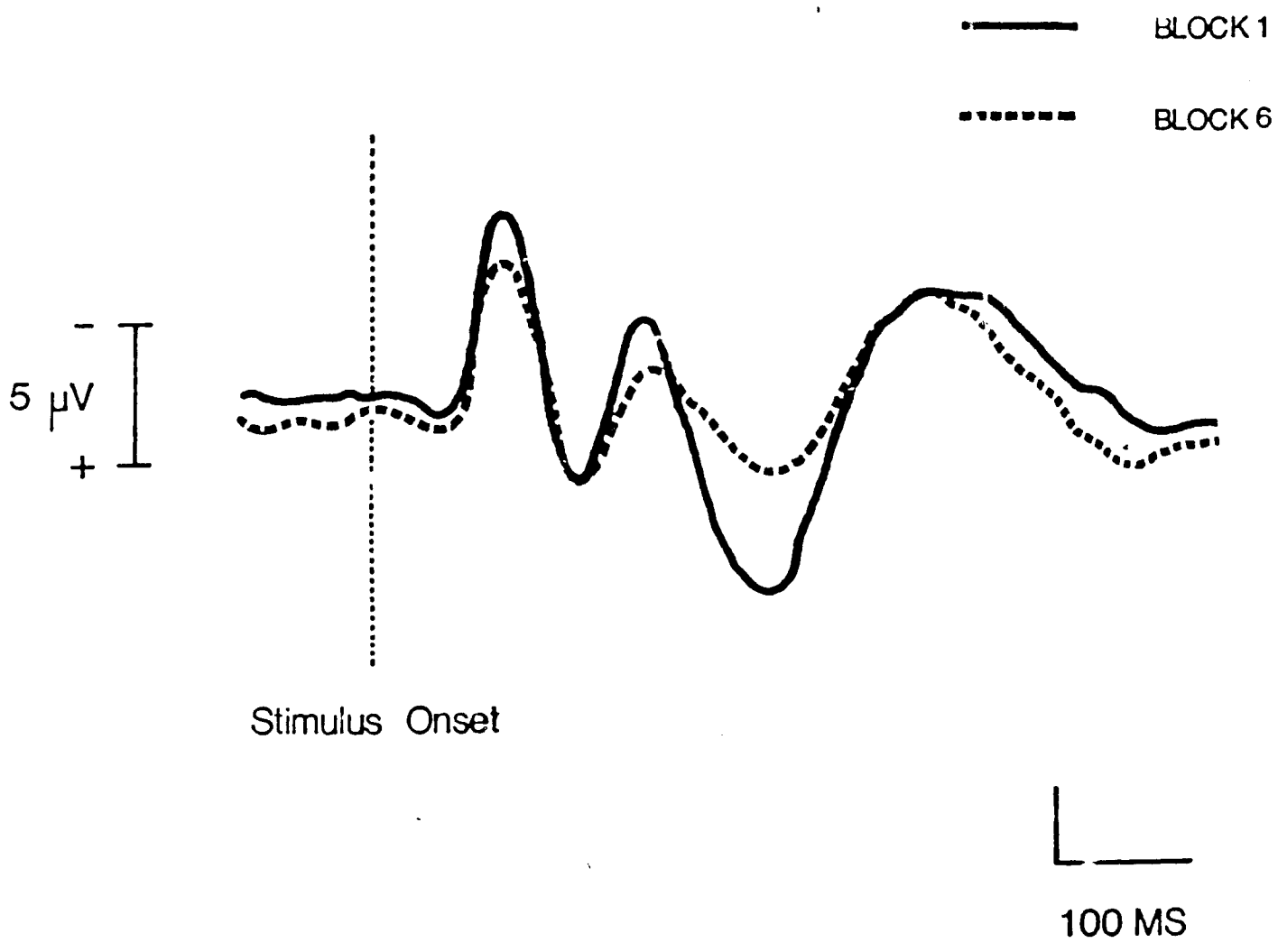

Figure 3. Averaged mean waveform for Block 1 versus Block 6.

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6.6 Experiment 6 - ERPs during the Wake/Sleep Transition

The questions addressed in this experiment were 1) What are the ERP changes associated with the Wake/Sleep transition? 2) Which of the ERP changes are associated with the decline in performance associated with the Wake/Sleep transition? and 3) What do the ERP changes tell us about changes in information processing during the Wake/Sleep transition?

During sleep, stimuli that normally elicit directed movement may no longer do so. Even those stimuli that signal the availability of goods or the presence of danger may not result in observable action. Reduced responsiveness is also associated with sleepiness. "Sleepiness" is a term often used in reference to the shortened sleep onset latencies associated with sleep loss, irregular sleep, and circadian factors.

Although progress has been made in describing decrements in responding related to sleep and sleepiness, little is known about the underlying processes. Sensory thresholds may be elevated, the capacity for information processing may be diminished, and/or the ability to select and organize responses may be depressed.

The present research concerns whether event-related brain potentials (ERPs) might provide useful information about the changes in responsiveness with sleep and sleepiness. The ERPs described here are scalp-recorded electrical potentials resulting from task-related stimulus presentation. ERPs reflect both psychological and physical properties of stimuli.

The research was motivated by the possibility that ERPs provide a reliable and unobtrusive index of information processing during sleep and sleepiness and might ultimately be useful in the assessment of performance readiness.

Method

Subjects Sixteen volunteer male and female students between the ages of 18 and 35 were tested in the sleep laboratory at the University of Southern Mississippi. The subjects were screened for health problems, medication use, and sleep/wake patterns. Informed consent was obtained and subjects were paid at the rate of $ 5/hr for their participation.

Apparatus Subjects were tested in a 9-ft by 13-ft room furnished with a bed and a straight-backed chair. Silver/silver chloride electrodes attached with electrode paste and collodion were used for the recording of all electroencephalographic (EEG) activity. The electrodes were referred to linked mastoids with a forehead ground. Impedances were kept below 5 KOhms. Additional electrodes were attached at the outer canthus and supraorbitally to the left eye for the recording of electrooculographic (EOG) activity. For the recording of sleep measures, electrodes were placed at C3 and O1 (International 10-20 Electrode Placement System; Jasper, 1958). Activity at these sites was amplified and filtered (using settings standard for sleep recordings) with Grass Model 7P511 amplifiers. Recordings of ERPs were obtained at Fz, Cz, and Pz of the 10-20 system and amplified and filtered using Colbourn High-gain Bioamplifiers. Low pass filtering was

accomplished using a software zero-phase digital filter set at 10.33 Hz. The high pass filter was bypassed and output was taken from the back of the amplifier for an effective fall time constant of 1.1 sec. The amplified data was digitized using an A/D board (Data Translation DT 2821) housed in a Compaq 386/25 computer. The EEG at Fz, Cz, and Pz was digitized (200 samples/sec) for 1500 ms with a 150 ms prestimulus baseline. Off-line averaging was controlled by a laboratory software program that included a software filter and a routine for the correction of ocular artifact (Gratton, Coles, & Donchin, 1983). Randomly alternating tones of 1000 Hz and 1500 Hz were presented binaurally (IST = 2 s) through miniature earphones taped in the subject's ears. For some subjects, the high-pitched tone and for other subjects the low-pitched tone was designated the "target". The target was presented on a random 20% of the tone presentation trials.

A response board was attached to the preferred hand of each subject and was used in conjunction with solid state equipment for the recording of fingerlift responses. The response board consisted of a hand-shaped piece of plywood to which was attached velcro straps and a photocell recording device that detected approximately 15 mm upward movements of the index finger (distance between plywood and photocell recording device: 25 mm). The response board was attached to the recording apparatus using cable that was light enough and long enough to permit the subject to adopt a preferred sleeping position with minimal discomfort. RT was digitized and recorded on an AT&T 6300 microcomputer.

Procedure Subjects arrived at the laboratory at an agreed upon late morning or early afternoon time. Subjects had reduced their sleep during the previous night by two to three hours and had sustained from caffeinated and alcoholic beverages for at least 24 hrs prior to the experiment. Subjects were randomly assigned to an experimental or a control group and briefed about the purpose of the study: to examine cortical evoked potentials during wakefulness and sleep. Subjects then signed an informed consent sheet and filled out a questionnaire about current health problems, the use of medication, and typical sleep pattern. After electrodes were attached, subjects were seated in a straight-backed chair in the laboratory and instructions were read to them by the experimenter. Subjects were told that one set of data would be collected while they were sitting in the chair with eyes open and one set while they were laying in bed with eyes closed and going to sleep. Experimental subjects were asked to keep a mental count of and make a fingerlift response to target tones. Nontarget tones were to be ignored. Subjects were told to continue to respond as long as possible but to not let sleep interfere with responding. Control subjects were instructed to ignore both target and nontarget tones. While sitting up, subjects were instructed to focus their eyes on a blue paper circle posted on the wall facing the subject to keep eye artifact at a minimum. Following instructions, subjects listened to a sample of high and low pitch tones. The experimenter then left

the room and the first set of tone presentations was initiated (25 targets). Following the first set, respiration belts were affixed on the abdomen and thorax and the subject was put to bed. The experimenter left the room and turned out the lights. Data were collected until the subject had remained in stage 2 sleep for a minimum of 10 continuous minutes.

Analysis Sleep records were scored in 30 s epochs following standard criteria (Rechtschaffen & Kales, 1968). ERPs were averaged for targets and nontargets during wakefulness, stage 1a (fragmented alpha), stage 1b (stage 1), stage 2a (first 5 min of stage 2), and stage 2b (first 5 min of stage 2 preceded by 5 min of continuous stage 2 sleep).

Results

Each stimulus presentation was classified according to sleep stage of occurrence and sleep-stage averages were obtained for target and nontarget stimuli at each lead for each subject. The data for one of the subjects tested under the Attend condition was unscorable. The grand averages of the ERPs obtained from the remaining seven subjects under the Attend and the eight subjects under the Ignore conditions are presented in Figures 1 and 2. For each subject and for each awake and sleep stage, the event potentials were computer scored using a peak picking program. Amplitudes and latencies were obtained for peaks located in windows determined by inspection of the averaged waveform for each stage.

ERPs During Wakefulness. As can be seen in Figures 1 and 2, a large (approximately 14 microV) P300 waveform was found in response to targets during the Attend condition. The mean latency of P300 was app. 360 ms. A smaller (less than 5 microV) parietal P300 can be seen (Figure 2) in the Ignore condition. A late frontal negativity of about 10 microV (mean latency = 525 ms was seen in response to the target under both the Attend and Ignore conditions. The P300 and the late frontal negativity were statistically comparable during Stage Wake and Stage 1A. N100 and P200 waveforms were scorable for both targets and nontargets under both Attend and Ignore conditions. N100 was maximal at Fz and had higher amplitudes and shorter latencies during the Attend condition. N100 latencies were shorter to targets. P200 was maximal at Cz and P200 latencies were also shorter to targets. N100 amplitude decreased and P200 amplitude increased during the progression from Stage Wake to Stage 1A. N200 could not be reliably scored in the data of each subject.

The Wake\Sleep Transition. Examination of Figures 1 and 2 suggests that sleep onset (Stage 1B) is associated with abrupt and dramatic changes in event potentials. Most striking was the reduction in the parietal P300 to the target stimuli under the Attend condition and the emergence for targets and nontargets under both Attend and Ignore conditions of a high-voltage negativity preceded and followed by lower amplitude yet prominent positivities. This P-N-P waveform was maximal at the Cz (vertex) lead and will be referred to here as the vertex potential.

Inspection of the data from each subject revealed that the emergence of vertex sharp waves to target stimuli under the Attend condition was closely related to response omissions. The data from two subjects illustrate this point. Figure 3 presents data from Subject 1. This subject, unlike the other subjects in the Attend condition, continued making fingerlift responses to the target stimulus throughout most of sleep stage 1 (scored here as Stage 1B). Shown in Figure 3 is ERPs averaged for stimuli presented in successive two-min intervals beginning with lights out. It can be seen that for Subject 1 the vertex sharp wave was not elicited and the awake P300-dominant ERP pattern continued for several minutes after onset of Stage 1B as defined by the EEG and also after sleep onset as defined by change in respiratory activity. For this subject, vertex sharp waves were not elicited by targets (spontaneous vertex sharp waves were evident in the EEG record) until just before Stage 2A. The appearance of the elicited vertex sharp wave was closely related to cessation of the behavioral response.

Unlike Subject 1, Subject 14 began missing targets while still awake. To show the relationship between vertex sharp waves and responding, ERP averages were obtained for Stages Wake and 1A based on the amplitude of negative-going activity in a scoring window from 300 ms to 450 ms. These averages along with the number of sweeps per average and the percent and average latency of behavioral responses are shown in Figure 4. It can be seen that even though scoring single sweeps is difficult because of noise, vertex sharp waves were closely related to response omissions.

Determinants of Vertex Sharp Waves. The amplitudes and latencies of the three deflections of the vertex sharp waves observed during Stages 1B, 2A, and 2B were analyzed using a Condition (Attend, Ignore) by Lead (Fz, Cz, Pz) by Tone (target, nontarget) by Sleep Stage (Stages 1B, 2A, 2B) analysis of variance. For all three deflections, the largest amplitudes and the shortest latencies were generally found at Cz, especially during Stages 2A and 2B. The waveform was smallest at Pz. These observations were supported by significant main effects for Lead or Lead by Stage interactions. Figure 5 presents the mean amplitude of the P-N-P deflections at Cz across Tones and Conditions during Stages 1B, 2A, and 2B. Mean values for P200, N200, and P300 measures obtained during Awake and Stage 1A are shown on the same coordinate system for comparison. Figure 6 shows mean latencies at Cz across Stage, Condition, and Tone.

Figures 5 and 6 show that the vertex sharp wave was influenced by instructions to attend to the stimulus presentations. As seen in Figure 6, peak latencies were shorter under the Attend condition relative to the Ignore condition. The Attend/Ignore differences were significant across leads and stages for the negative peak (N) and the second positive peak (P_2). For the initial positive peak (P_1), significant differences were found at Cz during Stage 2A and 2B only. The instructions to attend also influenced amplitude measures. The

amplitude of the negative peak was greater under the Attend condition at Cz for both targets and nontargets. The amplitude of P200 also tended to be generally higher during Stage 2A at the Cz lead.

The characteristics of the vertex sharp wave were also related to the eliciting stimulus (target vs nontarget). Stimulus probability effects are indicated by target/nontarget differences that are apparent under both the Attend and Ignore conditions. Target/nontarget differences in the amplitude of the P_1 and N components were apparent under both Attend and Ignore conditions with the lower-probability target stimulus eliciting the higher amplitude (see Figures 1, 2, 5, & 6). A main effect for Tone was found for the negative peak. Target/nontarget comparisons of P_1 amplitude under the Ignore condition made necessary by a significant Tone by Stage by Condition interaction, were significant. The Lead by Tone by Stage interaction for P_2 approached significance. Figure 5 indicates that for P_2 a target/nontarget amplitude difference at Cz in the Ignore condition was apparent in Stage 1B, but diminished as sleep progressed.

Inspection of Figure 5 indicates that target/nontarget differences in the amplitudes of the positive and negative components of the vertex sharp wave were greater, at least during some sleep stages, under the Attend than the Ignore condition. This observation was supported by a significant Tone by Stage by Condition interaction for P_1; however, no interactions involving Stage and Condition were significant for N or P_2.

Other ERP Changes. Additional evidence of task-relevance effects in sleep can be seen in Stage 1 (see Figures 1 & 2). There is a prominent frontal negative slow wave with an average latency of about 600 ms and average amplitude of approximately 13 microV at Fz in response to targets but not nontargets in the Attend condition only. This slow negativity was not evident in Stages 2A and 2B and may be related to the slow frontal negativity apparent in Awake and Stage 1A (see Figure 1).

Finally, task-relevance effects can be seen in a late slow positivity (P900) that is apparent in both the Attend and Ignore conditions during Stages 2A and 2B, but is of considerably greater amplitude in response to targets during the Attend condition (see Figures 1 & 2). Statistical analysis confirmed both the task relevance effect and the Lead effect. Analysis of the latency of the waveform revealed a shorter peak latency frontally (approximately 900 ms). There were no further significant effects for latency.

Additional stimulus probability effects were found in analysis of a frontal negativity (N550) that gradually became visually apparent in Stages 2A and 2B. The maximum amplitude of this waveform was at Fz as was the shortest peak latency.

Discussion

There are several statistically-reliable and important features of the present data including 1) During wakefulness, P300 at Pz is larger for the target stimulus under the attend

condition replicating much previous work; 2) N100 amplitude diminishes and P200 amplitude increases with sleep onset; 3) a prominent frontal negativity achieves maximum amplitude at stage 1B, then diminishes with sleep onset; 4) very pronounced changes in ERPs from wakefulness to sleep include a reduction in P300 amplitude and a pronounced vertex potential; 5) differences in target and nontarget ERPs during stage 2 include a larger vertex potential and also a late centrally-dominant target positivity (800-1000 ms); 6) target ERPs for the control subjects more closely resemble nontarget ERPs; and 7) behavioral responsiveness (both likelihood and latency of responding) was correlated with P300 and the vertex potential.

Previous studies have shown wake/sleep differences in ERPs to nonmeaningful stimuli. The present findings provide a description of ERPs to both meaningful and nonmeaningful stimuli during the transition from wakefulness to sleep. The findings with the nonmeaningful stimuli in the Ignore condition replicate and extend the earlier findings. The findings with the meaningful stimuli (Attend condition) provide further information about changes in event potentials and provide a basis for hypothesizing about the changes in cognitive processes during sleepiness and sleep. Thus the close correspondence between the gradual disappearance of parietal P300 and behavioral responding suggests that the reduced behavioral responsiveness is associated with and perhaps because of a change in cognitive processes. It is not clear what these changes may be. P300 has been associated with memory function and reduced capacity for stimulus evaluation and classification may be involved. On the other hand, it is arguable that what is lost during sleepiness and sleep is a more primitive function perhaps associated with stimulus detection or recognition. The findings of the present study suggest that sleepiness and sleep onset are associated with increases in the time required for stimulus detection and/or evaluation and classification and that performance decrements are due at least in part to the changes in these processes.

With regard to the waveforms recorded during sleep, the finding that ERPs differed between Attend and Ignore conditions and between targets and nontargets in the Attend condition argues for information processing during sleep. This is consistent with previous reports (cf. Sams et al., 1983; Wesensten & Badia, 1988). However, the present study does not clearly establish that the ERPs recorded in sleep and sleepiness can be interpreted in the same manner. Further research is needed to evaluate the comparability of the determinants of wake and sleep ERPs.

The close correspondence observed in this study between ERPs and behavioral responsiveness suggests encourages the view that ERPs provide a neurophysiological index of performance readiness. Most previous efforts to monitor performance readiness using neurophysiological measures have involved the use of ongoing EEG measures involving alpha and beta activity etc. Performance was found to deteriorate with EEG indicators of sleep. The present research indicates the ERP measures may provide more accurate

information about readiness to respond. That is, the ERPs were related to performance changes of subjects who were missing responses while awake and of those subjects who were continuing to respond during sleep.

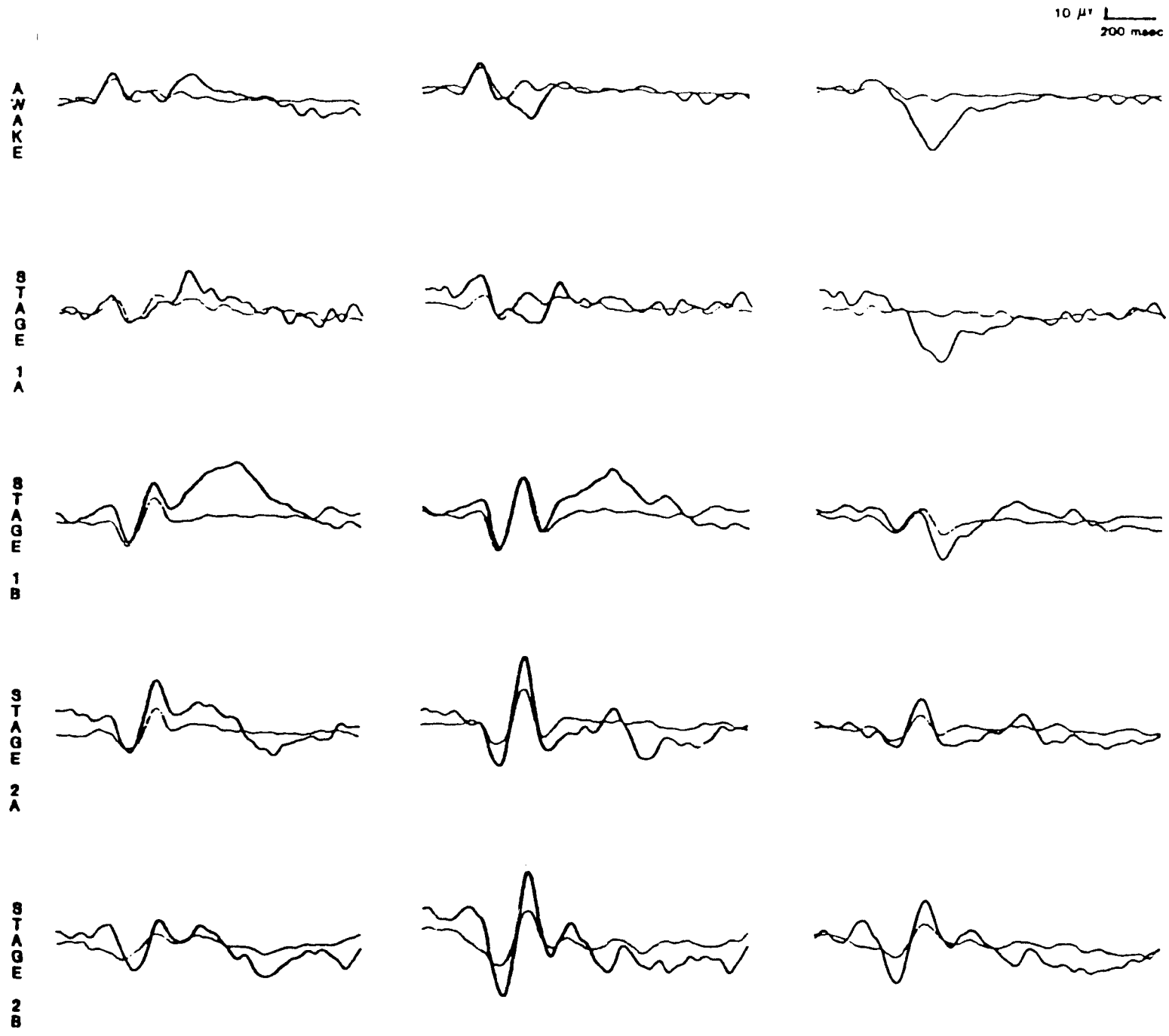

Figure 1 - Grand average ERPs for Experimental subjects

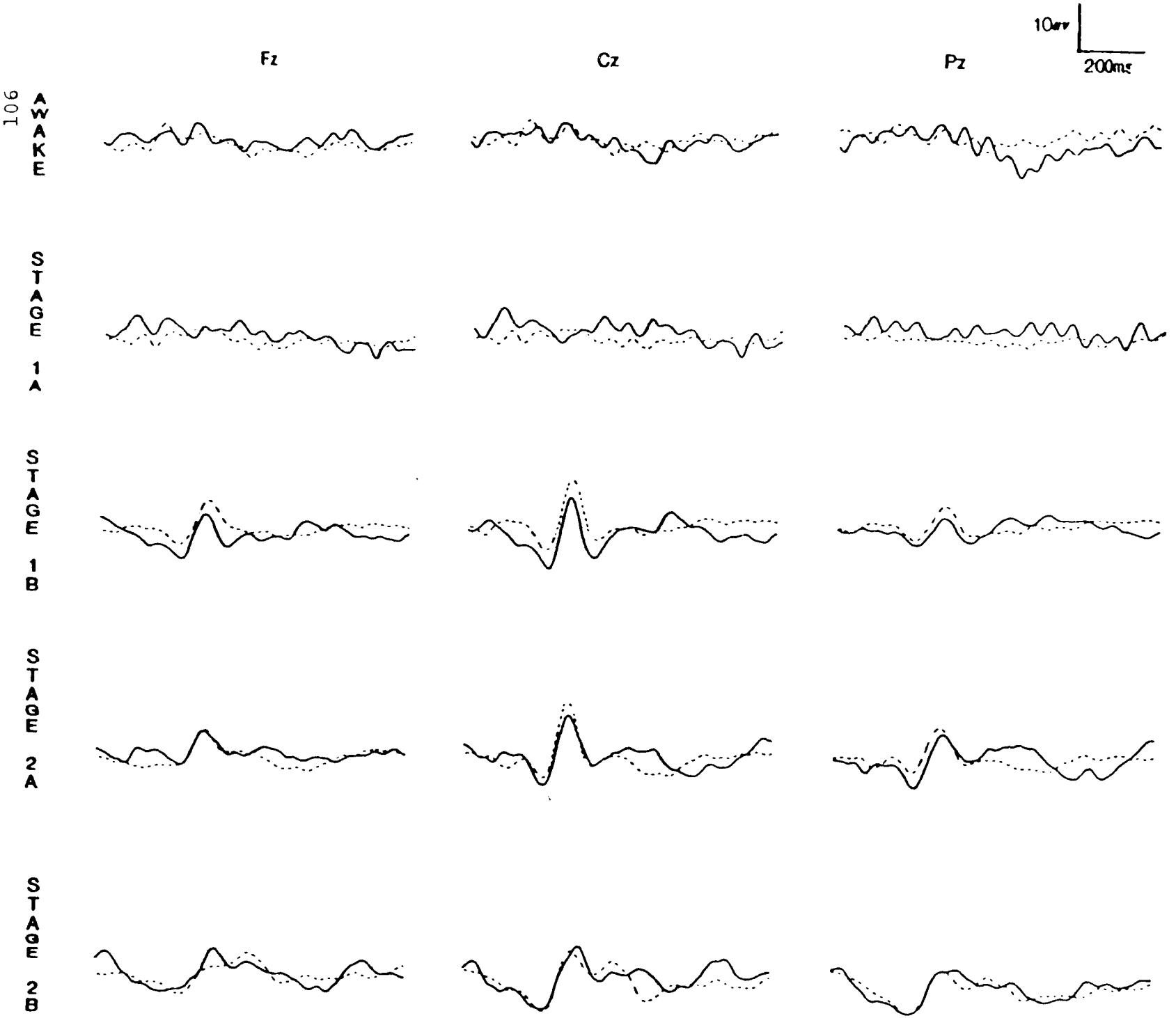

Figure 2 - Grand averages ERPs for Ignore condition

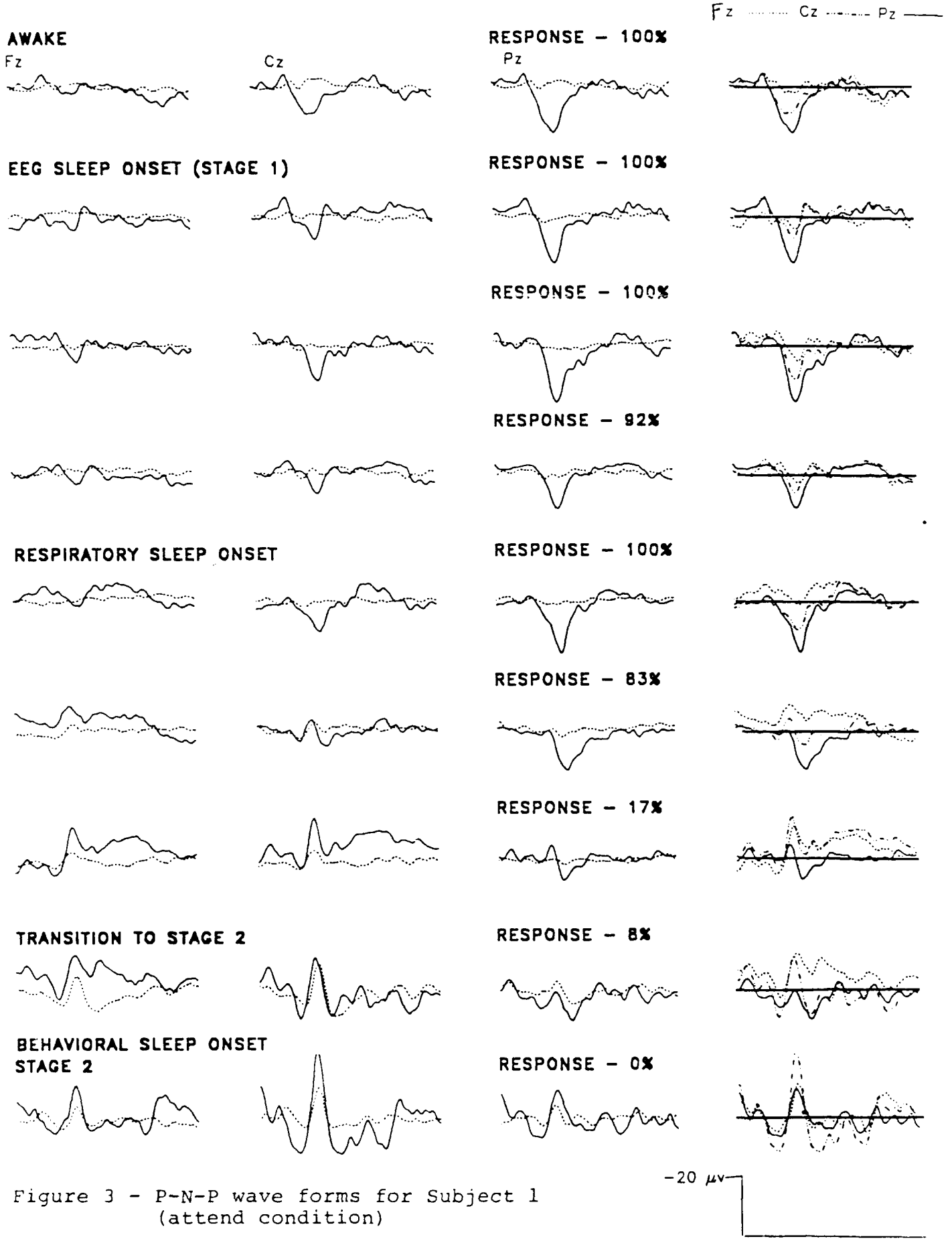

Figure 3 - P-N-P wave forms for Subject 1 (attend condition)

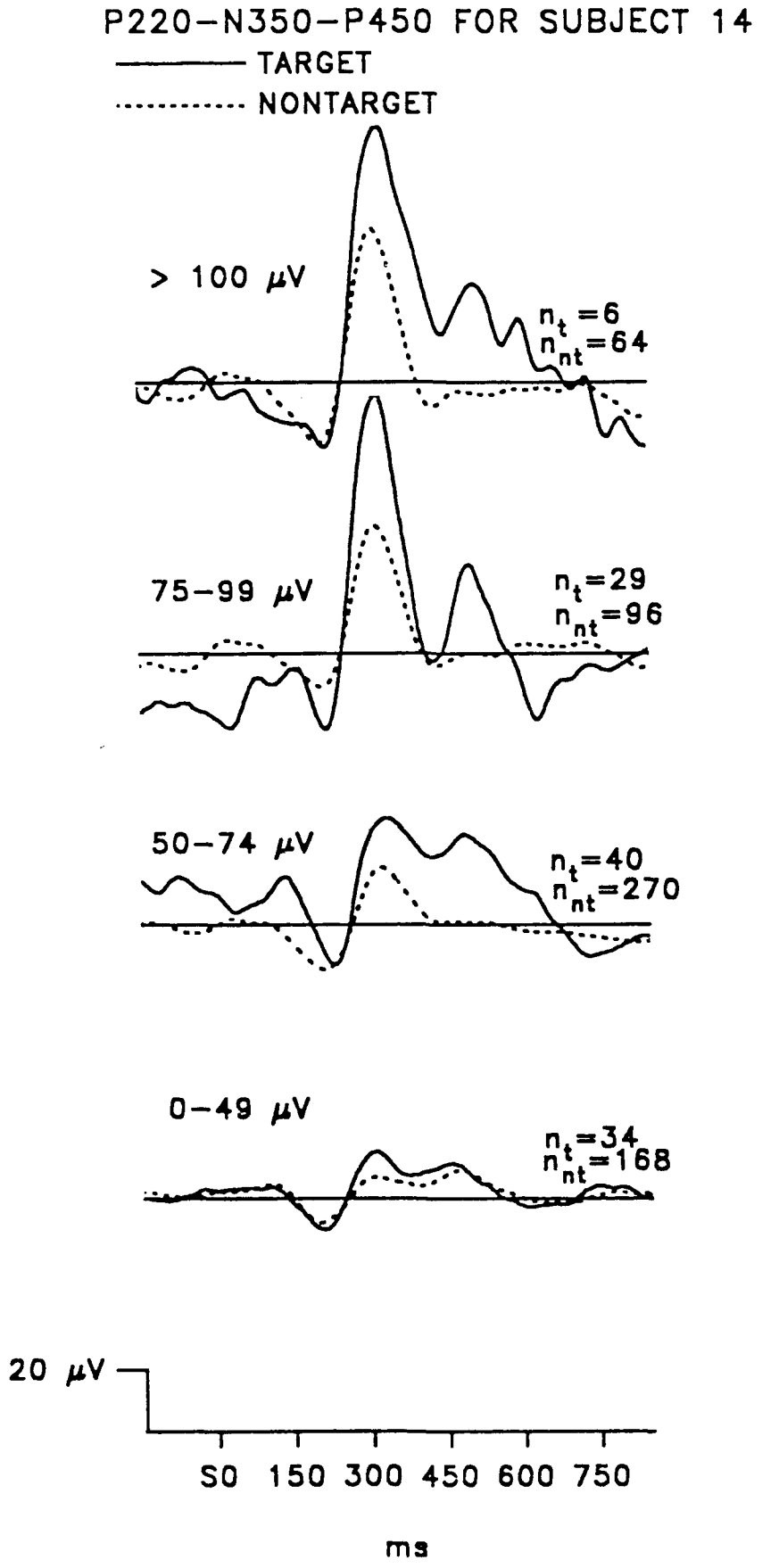

Figure 4 - P-N-P Waveforms for Subject 14 (Attend Condition)

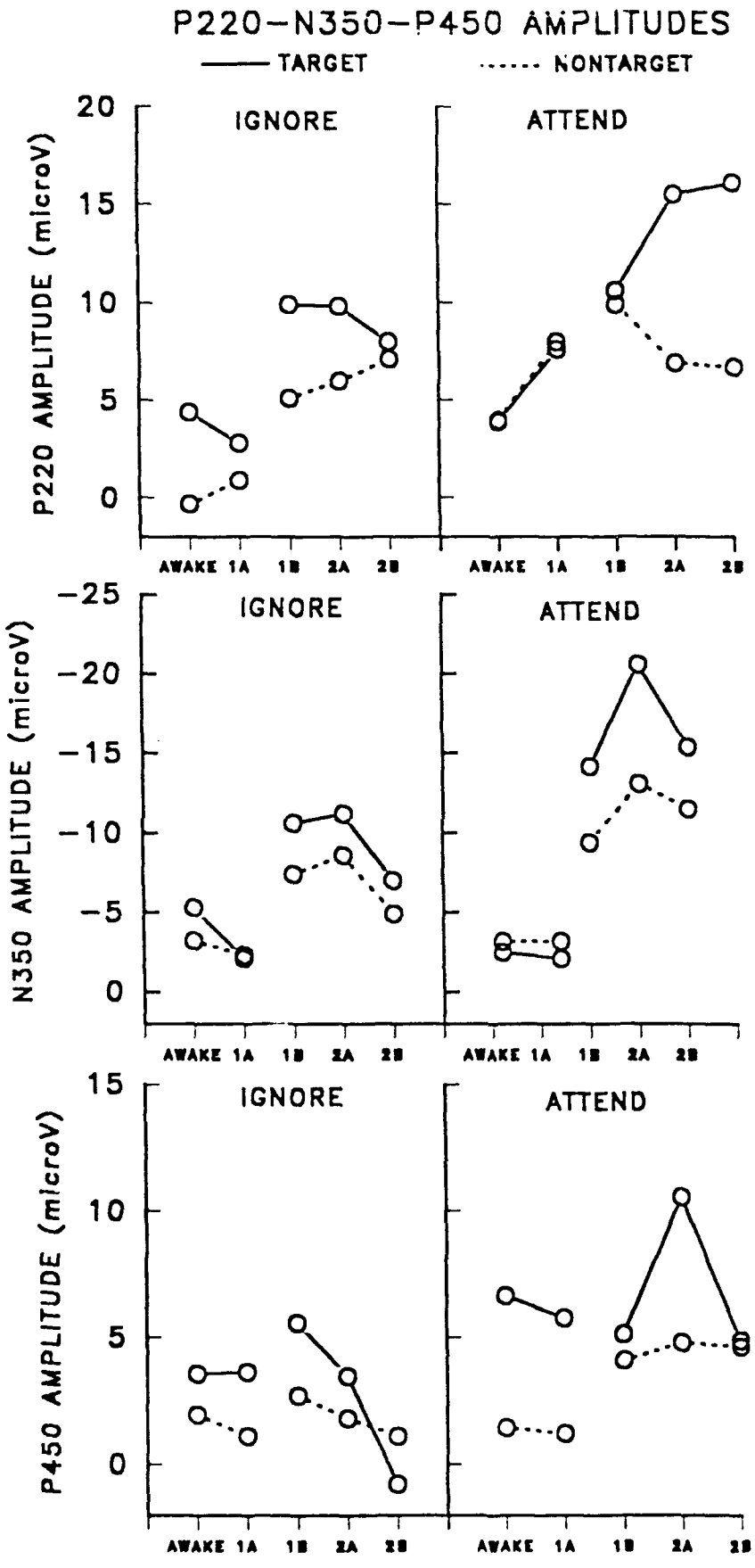

Figure 5 - Average P-N-P Amplitudes

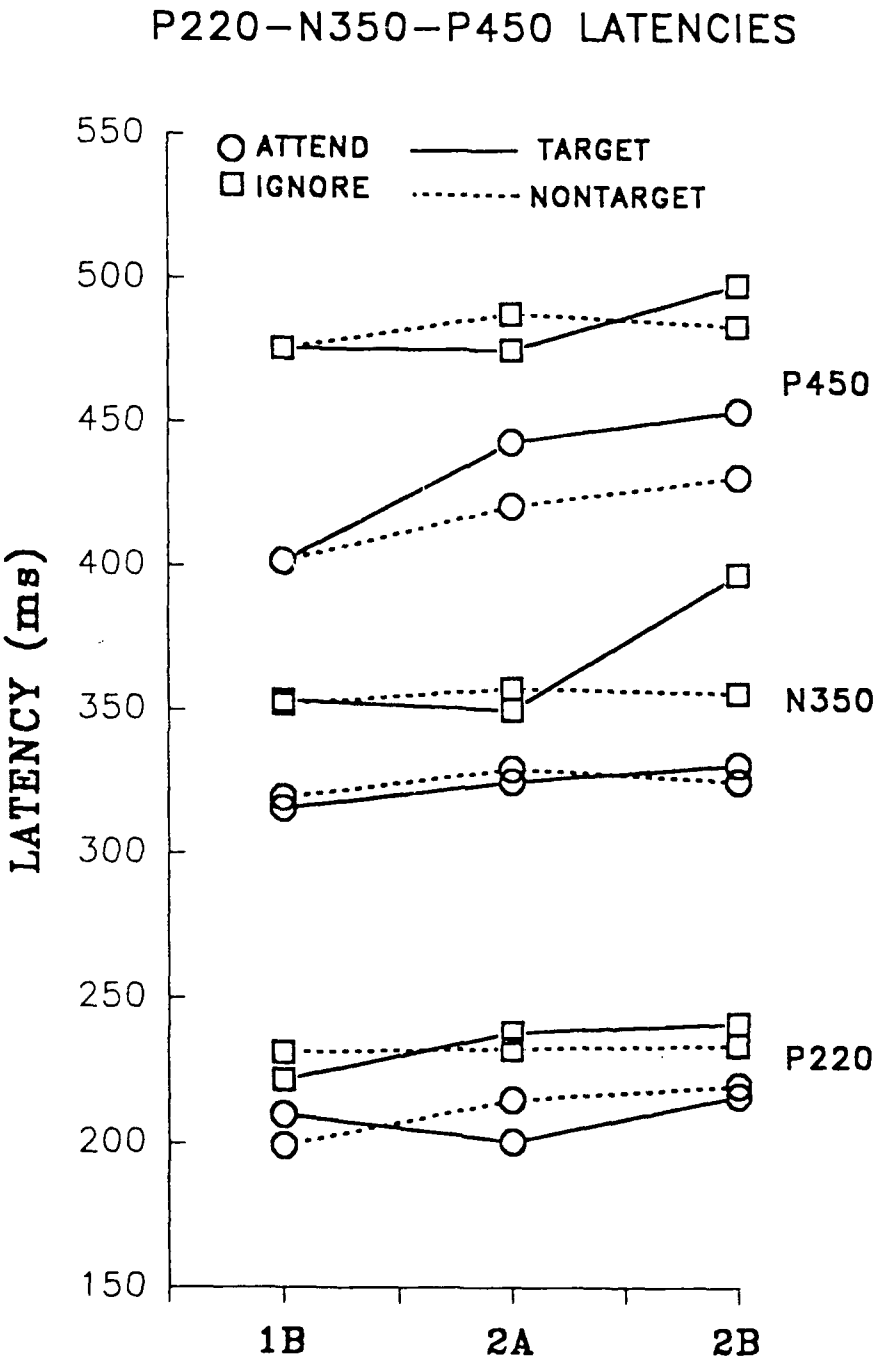

Figure 6 - Average P-N-P Latencies

References for Experiment 6

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6.7 Experiment 7 - ERPs During the Wake/Sleep Transition Using a Missing Stimulus Procedure.

Experiment 6 revealed quite profound changes in ERPs during the wake/sleep transition. The changes were most dramatic for target stimuli under the Attend condition. Thus, during wakefulness, the dominant feature of the target ERP was a parietally maximal P300 waveform. During sleepiness and sleep, however, a large centrally-dominant vertex potential emerged. This potential was closely related to changes in behavioral responsiveness. It is not clear what this change means in terms of changes in cognitive processes. The negative peak of the vertex potential and the following positivity may reflect the same processes as N200 and P300 during wakefulness. On the other hand, the P-N-P vertex potential may be a unitary phenomenon reflecting not a cognition, but some sort of arousal-related mechanism activated at about the time of sleep onset. Experiment 6 provided some information on this issue in that the vertex potential varied as a function of instructional conditions (Attend vs Ignore) and stimulus type (target/nontarget). That is, the vertex potential was found to be determined by the "psychological" charateristics of the eliciting stimulus.

Experiment 7 continued the analysis of the psychological determinants of the vertex potential. Specifically, the conditions of Experiment 6 were replicated with the exception that the target stimulus under the Attend condition was not a physical stimulus, rather the omission of the nontarget stimulus. This omitted stimulus procedure permits studying the ERPs to a stimulus having no physical characteristics thus permitting the study of the components of ERPs produced by the psychological significance of an event.

Method

Subjects Sixteen volunteer male and female students between the ages of 18 and 35 were tested in the sleep laboratory at the University of Southern Mississippi. The subjects were screened for health problems, medication use, and sleep/wake patterns. Informed consent was obtained and subjects were paid at the rate of $ 5/hr for their participation.

Apparatus Subjects were tested in a 9-ft by 13-ft room furnished with a bed and a straight-backed chair. Silver/silver chloride electrodes attached with electrode paste and collodion were used for the recording of all electroencephalographic (EEG) activity. The electrodes were referred to linked mastoids with a forehead ground. Impedances were kept below 5 KOhms. Additional electrodes were attached at the outer canthus and supraorbitally to the left eye for the recording of electrooculographic (EOG) activity. For the recording of sleep measures, electrodes were placed at C3 and O1 (International 10-20 Electrode Placement System; Jasper, 1958). Activity at these sites was amplified and filtered (using settings standard for sleep recordings) with Grass Model 7P511 amplifiers. Recordings of ERPs were obtained at Fz, Cz, and Pz of the 10-20 system and amplified and filtered

using Colbourn High-gain Bioamplifiers. Low pass filtering was accomplished using a software zero-phase digital filter set at 10.33 Hz. The high pass filter was bypassed and output was taken from the back of the amplifier for an effective fall time constant of 1.1 sec. The amplified data was digitized using an A/D board (Data Translation DT 2821) housed in a Compaq 386/25 computer. The EEG at Fz, Cz, and Pz was digitized (200 samples/sec) for 800 ms with a 150 ms prestimulus baseline. Off-line averaging was controlled by a laboratory software program that included a software filter and a routine for the correction of ocular artifact (Gratton, Coles, & Donchin, 1983). Randomly alternating tone (1000 Hz) and no tone trials were presented (ISI = 1 s). The tones were presented binaurally through miniature earphones taped in the subject's ears. The target (stimulus omission) was presented on a random 10% of the trials.

A response board was attached to the preferred hand of each subject and was used in conjunction with solid state equipment for the recording of fingerlift responses. The response board consisted of a hand-shaped piece of plywood to which was attached velcro straps and a photocell recording device that detected approximately 15 mm upward movements of the index finger (distance between plywood and photocell recording device: 25 mm). The response board was attached to the recording apparatus using cable that was light enough and long enough to permit the subject to adopt a preferred sleeping position with minimal discomfort. RT was digitized and recorded on an AT&T 6300 microcomputer.

Procedure Subjects arrived at the laboratory at an agreed upon late morning or early afternoon time. Subjects had reduced their sleep during the previous night by two to three hours and had sustained from caffeinated and alcoholic beverages for at least 24 hrs prior to the experiment. Subjects were randomly assigned to an experimental or a control group and briefed about the purpose of the study: to examine cortical evoked potentials during wakefulness and sleep. Subjects then signed an informed consent sheet and filled out a questionnaire about current health problems, the use of medication, and typical sleep pattern. After electrodes were attached, subjects were seated in a straight-backed chair in the laboratory and instructions were read to them by the experimenter. Subjects were told that one set of data would be collected while they were sitting in the chair with eyes open and one set while they were laying in bed with eyes closed and going to sleep. Experimental subjects were asked to keep a mental count of and make a fingerlift response to targets. Nontarget tones were to be ignored. Subjects were told to continue to respond as long as possible. Control subjects were instructed to ignore both target and nontarget trials. While sitting up, subjects were instructed to focus their eyes on a blue paper circle posted on the wall facing the subject to keep eye artifact at a minimum. Following instructions, subjects listened to a sample of trial presentations. The experimenter then left the room and the first set of trials was initiated (25 targets). Following the first set, respiration belts were affixed

on the abdomen and thorax and the subject was put to bed. The experimenter left the room and turned out the lights. Data were collected until the subject had remained in stage 2 sleep for a minimum of 10 continuous minutes.

Analysis Sleep records were scored in 30 s epochs following standard criteria (Rechtschaffen & Kales, 1968). ERPs were averaged for targets and nontargets during wakefulness, stage 1a (fragmented alpha), stage 1b (stage 1), stage 2a (first 5 min of stage 2), and stage 2b (first 5 min of stage 2 preceded by 5 min of continuous stage 2 sleep).

Results

The grand averages of the ERPs obtained in the Attend and Ignore conditions are shown in Figures 1 and 2, respectively. During wakefulness under the Attend condition, it can be seen that there is a prominent target N200 Cz, and a target P300 at Pz. The rather small N200 amplitude is, at least in part, due to latency jitter, as demonstrated in Figure 2.

During the wake/sleep transition period (Stages 1A, 1B, & 2A), N200 and P300 amplitudes were greatly attenuated (see Figures 1, 3, & 4). During sleep (Stage 2B), a large negativity at about N200 latency and a positivity at about P300 latency emerged prominently at Cz. The latency of the sleep negativity was not significantly different from the latency of the wake N200 (Figure 3).

Under the Ignore condition (Figure 2), a small N200 is observable in the awake condition at Cz; P300 is not distinguishable. During the wake/sleep transition, the nontarget waveform resembles that seen during the Attend condition. There was no consistent waveform apparent to the target event (stimulus omission) during the wake/sleep transition.

Discussion

The data obtained during the Attend condition during wakefulness replicates our previous findings. That is, a centrally dominant N200 and a parietally dominant P300 were found in response to the omitted stimulus. Data obtained during the wake/sleep transition also replicates previous findings in that the parietal P300 faded during sleep while a prominent negativity emerged during sleep to the nontarget tone stimuli.

As in Experiment 6, we found a large sleep-related negativity to targets that was prominent at Cz. The fact that this negativity occurred in response to an omitted stimulus provides strong evidence for the psychophysiological significance of the deflection. The Attend/Ignore differences further strengthens this interpretation. The N-P complex during sleep may reflect the operation of a mismatch detector which signals a change in background stimulation (cf. Snyder & Hilyard, 1976).

The significance of the reduced target/nontarget differences and the overall "flatness" of the target ERP during Stage 1B and 2A observed in the present as well as in earlier of our studies is not clear. One possibility is that this marks a neurophysiologically-distinct period of sleep onset associated with hypnogogia and related phenomena.

200ms
10uv
Pz
Cz
Fz
AWAKE
STAGE 1A
STAGE 1B
STAGE 2A

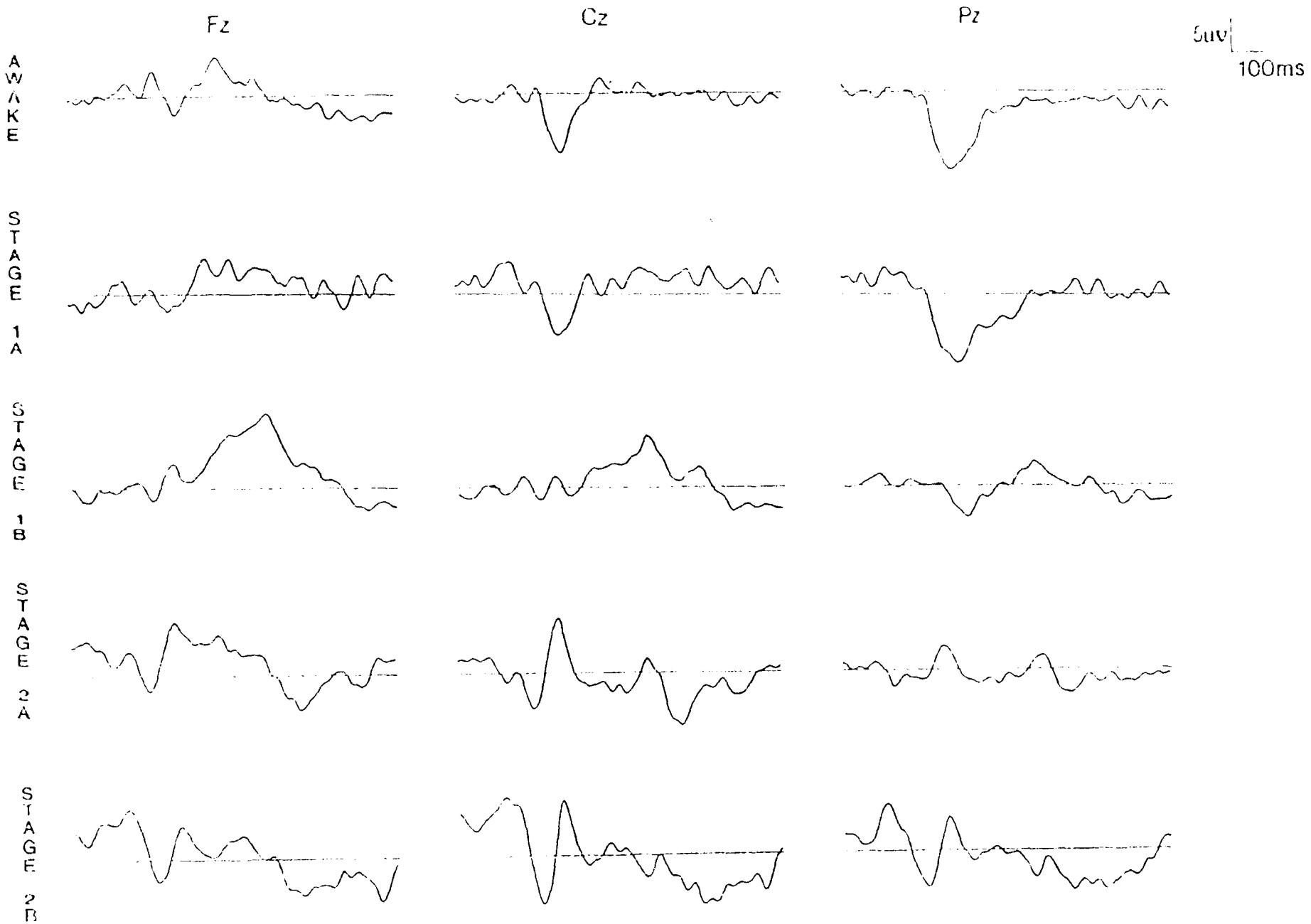

Figure 2 - Grand Average ERPs for Ignore Condition

References for Experiment 7

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Wesensten NJ, Badia P. (1988) The P300 component in sleep. Physiol. Beh. 44, 215-220.

6.8 Experiment 8 - Probability and Task Relevance as Determinants of ERPs During Wakefulness and Sleep

The purpose of this study was to examine the effects of stimulus probability on evoked potentials in wakefulness, sleep, and the transition from wakefulness to sleep, in order to learn if the underlying processes responsible for ERP components in sleep are similar to the processes responsible for ERP components in wake. If ERPs behave similarly in sleep and in wakefulness, they may be used to gain information about the processes associated with the decreased responsivity found in sleep. For example, components of ERPs in wakefulness are believed to be reflections of stimulus evaluation processes. If ERPs in sleep are a reflection of the same processes, the study of ERPs in sleep may give us information about stimulus evaluation in sleep.

In this study, there were three levels of target probability, .20, .50, and .80. Differences in target/nontarget ERPs were expected at unequal probability levels based on past studies of probability effects on ERPs.

At the .20 probability level differences were expected between targets and non-targets during wakefulness, ERP amplitudes to targets being larger. In their study on the effects of probability on the P300 in wake, Duncan-Johnson and Donchin (1977) found that P300 was prominent when the tone was rare (when it's probability was less than .30) regardless of it's target or non-target status. However the P300 was higher to the targets than that to the non-targets at the corresponding level of probability. The greater amplitude to the target stimuli is considered to be a result the task-relevance of the targets Donchin et al. 1986). Thus, P300 amplitude reflects both probability effects and cognitive processing demands. During sleep, N200 was expected to show a dramatic increase in amplitude, and P300 was expected to shift in latency. Whether there would be probability effects, or differences between targets and non-targets was not known. The results of the Wesensten & Badia (1988) study indicate that probability effects persist in sleep; however this has not been replicated.

At the .50 probability level during wakefulness, differences between targets and non-targets were expected due to the task relevant nature of the targets. During sleep, task relevance has been reported to be a factor (Wesensten & Badia, 1988), but unlike wake, the late positivities reported to show the task-relevant effects have been reported when the stimuli are not task-relevant. It was not felt that enough information was currently available to make a prediction about target/non-target differences at this level of probability.

At the .80 probability level differences were expected between targets and non-targets during wakefulness, ERP amplitudes to non-targets being larger due to the effects of probability. The results of the Wesensten & Badia (1988) study supported the hypothesis that probability differences would

persist in sleep at this level; however no predictions were made.

By examining the influence of probability on ERPs to task relevant stimuli during the transition from wakefulness to sleep, the involvement of task-relevance and attention during this transition was studied through the interaction with probability. Sleep is characterized by a decrease in responsivity to external stimuli. Task relevance and attention were measured by the subject's response to the target stimulus. While responding to stimuli in wakefulness indicates that the subject is attending, and the cessation of responding indicates that the subject is no longer attending, it is not known what processes are responsible for the cessation of responding during sleep. The decrease in responsivity may be affected by reductions in capacity to evaluate stimuli, reductions in the capacity to select and emit responses, and/or reductions in motivation (Harsh & Badia 1989). This decrease in responsivity may be an indication that the stimuli have lost significance to the subject, and are no longer task relevant, or that the stimuli still have meaning for the subject, but they no longer respond for some reason.

If probability effects persisted in sleep, this would be evidence for 1) the persistence of task-relevance during sleep, or 2) that probability effects occur in sleep independent of task-relevance. If target/non-target differences were found at corresponding levels of probability, this would indicate that task relevance is a factor influencing ERPs in sleep, and if these differences persisted to missed targets, this would be evidence that discrimination continues during sleep after behavioral responding stops. If no probability differences were seen, this would be evidence that the N200 and P300 reported in wake and sleep are reflections of different processes.

METHOD

Subjects Ten subjects, ages 18-35, were recruited from the student population at the University of Southern Mississippi. They were screened for health problems, medication use, and abnormal sleep-wake schedules. An informed consent was signed by all subjects. Subjects were paid $25.

Apparatus All subjects were tested in a 9 ft by 13 ft room and were monitored throughout the experiment with an infrared camera and lighting system. ERP and EEG signals were collected through silver/silver chloride electrodes affixed to the scalp in standard placements (International 10-20 Electrode Placement System; Jasper, 1958). Electrode impedances were below 10,000 ohms. EEG (O1 and C3), EOG, and EMG channels were recorded on a Grass Model 78-D polygraph, and scored for sleep according to standard criteria of Rechtschaffen and Kales (1968). ERPs were collected from Fz, Cz, and Pz electrode placements and referenced to linked mastoid placements. EOG electrode placements were above and below either eye. Eye blink artifact was subtracted from averaged ERPs (Gratton, Coles, & Donchin, 1983). ERP signals were amplified using Coulbourn High-gain Bioamplifiers and signals were digitized and stored on a Compaq 25/386 microcomputer. Coulbourn amplifier low-cutoff filters were

bypassed, and output was taken from the back of the amplifier for an effective fall time constant of 1.1 sec. Coulbourn amplifier hi-cutoff filters were bypassed, and hi-filtering was accomplished using a software zero phase digital filter using a moving average technique (Ruchkin & Glaser, 1989) for an effective hi-filter frequency of 10.33 hertz. Coulbourn amplifier gain was set at 10,000. Tone presentations were controlled by Coulbourn Instruments equipment. Tones were presented binaurally through miniature headphones in a Bernoulli series. Target tones (p = .2, .5, .8), were set at either 1000 Hz or 1500 Hz (counterbalanced from subject to subject). Nontarget tones (p = .8, .5, .2) were set at the frequency not selected for targets (1000 Hz or 1500 Hz). Interstimulus interval was 1.5 seconds. Tone intensity was 60 dB (SPL), and tones were presented against a continuous background of white noise at 65 dB. Reaction time was measured by a device strapped to the subjects preferred hand. To respond, the subject lifted his index finger to break a photoelectric beam. Reaction time was digitized and recorded on an AT&T 6300 microcomputer.

Procedure The subjects were instructed to sleep deprive themselves for 3 hours the nights before testing, and not to nap any on the previous day or on the day of the test. They were asked to abstain from drugs and alcoholic beverages, and not to take in excessive caffeinated beverages during the 3 days before testing, until the experiment is completed, and were told to be prepared for testing which will last most of the day. Subjects were telephoned the night, and the morning before testing to insure sleep deprivation.

Testing was conducted on Saturdays and Sundays. Subjects reported to the Sleep Laboratory on the test day at 1100 hours. The electrodes were then applied. After hookup, the subjects laid down, the procedure was reviewed, and the testing began. The subject was instructed to ignore the "non-target" tones and to make a finger-lift response to the "target" tones. They were further instructed to not fight off sleep in order to continue responding. The first trial consisted of 25 target tones at the initial testing probability (counterbalanced from subject to subject), and the accompanying nontarget tones while the subject remained in the chair awake. The second two trials consisted of 25 target tones at the initial testing probability, and the accompanying nontarget tones while the subject remained in the bed awake. The subject was then instructed to continue to respond to the tones, and to go to sleep. Tones were continuously presented until the subject had been in stage 2 sleep for 10 minutes. Three sets of trials were presented in this fashion. At the end of each set, the subject was awakened and instructed to get out of bed and remain awake for 20 minutes before beginning the next set. The target probabilities for these three sets were 20%, 50%, and 80% with the order counterbalanced from subject to subject. After three successful sleep sets, one at each probability, the experiment was terminated. If any problems prevented collecting data at all

three probability levels, testing was continued for another day to collect the needed data.

Analyses

Each evoked potential was corrected for removal of eye blink artifact using a computer algorithm (Gratton et al., 1983). Polygraph recordings were scored for sleep stages using standard criteria of Rechtschaffen, and Kales (1968). Target and nontarget ERPs were averaged for sleep stages Sitting Awake, Supine Awake, 1, 2a, and 2b at each level of probability. The averaged ERPs were then baseline adjusted by subtracting the average of the prestimulus baseline points from the remaining ERP points. Peaks for target waveforms were scored by a computer program which picks the lowest or highest peak within the specified time window. Waveforms N100, N200, and P300 were scored for amplitude and latency. The following windows were defaults used for wake waveforms: N100 - 70-130 msec; N200 - 200-400 msec; P300 - 300-600 msec. All ERP waveforms were visually inspected before peak scoring, and the windows were adjusted as necessary when a waveform fell outside the scoring window, or latencies shifted. Earlier components were identified first in temporal order, (e.g., P100, N100, and P200 respectively). N200 was identified as the first negative component appearing after P200. The P300 was identified as the next positive component following N200. Nontarget waveforms were measured for amplitude at the same latency as the corresponding targets.

Results

Throughout the results section probability condition refers to the set of ERPs collected during one condition. The probability conditions are labeled by the target probability. Thus, the P2 condition refers to the condition with targets at a probability level of .2. Since the target and non-target probabilities add to 1.0, non-targets during the P2 condition are at a probability level of .8.

ERPs were analyzed for five stages. Awake-Sitting refers to ERPs obtained while the subjects were awake and sitting in a chair (the subjects were instructed to keep their eyes open). Awake-Supine data were obtained while the subject was in bed but still in stage Wake according to standard (Rechtschaffen & Kales, 1968) sleep scoring criteria. Stage 1 was also scored using standard criteria. Stage 2a refers to the first five minutes of uninterrupted Stage 2. Stage 2b refers to subsequent uninterrupted Stage 2 sleep (up to five minutes).

All variables were analyzed using repeated measures analysis of variance using the BMDP4V statistical software program (Dixon, 1985). All *F* ratios were adjusted using the Huynh-Feldt correction procedure for repeated measures. Where appropriate, the Newman-Keuls post-hoc procedure was used to clarify differences in means.

Reaction Time

Reaction time speed and response probability were analyzed using a Stage (5) by Probability (2) analysis of variance. Figure 1 shows speed of responding (reciprocal of response time) across

probabilities and stages. Missed responses were assigned a maximum value of 1100 ms. Figure 1 suggests that the time required for subjects to respond to the target presentations depended on both sleep stage and target probability. The analysis of variance supported these observations yielding a main effect for Stage, $F(2.03/14.18)=76.17$, $p<.001$, and a Stage by Probability interaction, $F(4.2/29.43)=2.88$, $p=.038$. An examination of the stage by probability interaction showed probability effects to be significant at Awake-Sitting only, $F(2/14)=4.38$, $p<.050$. Inspection of means indicates that reaction time speed values for the P2 and P5 conditions (2.415, and 2.428) are shorter than those for the P8 condition (2.854), however post-hoc comparisons failed to reveal any differences.

Figure 2 shows response probability across stages. Response probability in all three probability conditions declined across stages, $F(4/28)=76.17$, $p<.001$. Post-hoc comparisons indicated that decreases were significant from Awake-Sitting ($p=.97$) to Awake-Supine ($p=.77$), from Awake-Supine to Stage 1 ($p=.23$), and from Stage 1 to Stage 2a ($p=.02$). Stages 2a and 2b ($p<.01$) were not significantly different from each other. The Probability and Stage by Probability interaction effects were not significant.

ERPs at Awake-Sitting

Grand averages of ERP waveforms for all levels of Stimulus, Probability, Stage, and Lead are included for reference in Figures 3, 4, and 5.

All latency and amplitude measures for ERPs at stage Awake-Sitting were analyzed using a Stimulus (target, non-target) by Lead (Fz, Cz, Pz) by Probability (P2, P5, P8) analysis of variance.

P300 Latency Figure 6 shows P300 latencies across probability condition for targets and non-targets during the Awake-Sitting condition. Figure 6 suggests that P300 latency depended on both stimulus type (targets or non-targets) and probability condition. Analysis of variance yielded a main effect for Stimulus, $F(1/7)=11.08$, $p=.013$, with targets showing a mean latency of 351 ms, and non-targets showing a mean latency of 372 ms. The Probability by Stimulus interaction approached significance, $F(2.00/14.00)=3.30$, $p=.067$. A-priori considerations justified looking at P300 latency for targets. Analysis of P300 latency for targets revealed a Probability effect, $F(2.00/14.00)=4.57$, $p=.030$. Inspection of means indicates that P300 latencies for the P2 and P5 conditions (360 ms, and 365 ms) are longer than those for the P8 condition (327 ms), however post-hoc comparisons failed to reveal any differences.

P300 Amplitude Figure 7 is a graph of P300 amplitude at each lead at each probability condition. As expected based on the results of several earlier studies, Target P300 amplitude increased as the targets became more rare, especially at Pz. It should be noted that at Pz, P300 amplitude was generally larger to targets, except at the P8 condition, were non-targets were larger. Consistent with this, the analysis of variance of P300 amplitude at awake-sitting showed a three way interaction between

Lead, Probability, and Stimulus, $F(4.00/28.00)=12.20$, $p<.001$. Amplitudes were largest at Pz for both targets and non-targets at all probabilities. Two-way analysis of variance of P300 amplitude at Pz yielded a Probability by Stimulus interaction, $F(2/14)=35.81$, $p<.001$, with both targets, $F(2/14)=24.59$, $p<.001$, and non-targets, $F(2/14)=3.82$, $p=.047$, showing a significant Probability effect. Post-hoc comparisons for targets indicated that all means were significantly different from each other, with amplitude significantly decreasing from the P2 condition (17.41 μv) to the P5 condition (10.71 μv), to the P8 condition (2.82 μv). For non-targets, amplitudes were greatest at the P8 condition (9.192 μv), followed by the P5 (6.500 μv) and P2 (4.717 μv) conditions. Post-hoc comparisons indicate that only the P2 and the P8 conditions were significantly different from each other. Thus, for both targets and non-targets, P300 amplitude was greatest when the stimulus was rare, and smallest when the stimulus was frequent.

A-priori considerations justified looking a Figure 9 and the results parallel those already discussed for Pz at Awake-Sitting (see ERPs at Wake section above).

At Stage 2b, Probability and Stimulus effects reappear. Probability is significant for targets, with P300 amplitude greatest at the P2 condition, followed by the P5 and P8 conditions. Amplitudes were 6.34 μv, 4.22 μv, and 1.44 μv respectively. For non-targets, P300 amplitude showed a general decrease from the P8 condition to the P2 condition, but this was not statistically significant. The Stimulus effect was significant at the P5 condition, $F(1/7)=9.10$, $p=.020$, with targets showing greater amplitude than non-targets. Amplitudes were 4.22 μv and -0.61 μv respectively. As can be seen in Figure 9, targets are larger than non-targets at equal probability levels for both awake stages and Stage 2b, except for the $p=.80$ level.

Lead effects are seen in Figure 9, P300 amplitude showing a parietal focus at Awake-Sitting and Awake-Supine, a central focus in stage 2a, and a central focus in 2b. Analysis of variance supported this showing a 2-way interaction for Stage and Lead, $F(2.96/20.70)=5.66$, $p=.006$. During Awake-Sitting and Awake-Supine, Pz is the focus for P300, and the effect for Lead is significant at each of these 2 stages (Awake-Sitting, $F(1.90/13.29)=19.42$, $p<.001$, and Awake-Supine, $F(1.76/12.35)=12.16$, $p=.002$). Mean amplitudes at Fz, Cz, and Pz, for stage Awake-Sitting were 3.754 μv, 6.931 μv, and 8.559 μv, and for Awake-Supine were 1.296 μv, 2.634 μv, and 3.633 μv, respectively. During the remaining 3 sleep stages, there are no main effects for lead, or lead interactions involving stage.

The Probability by Stimulus by Lead interaction was significant, $F(3.63/25.44)=5.42$, $p=.003$, with the Stimulus by Probability interaction significant at Fz, $F(1.57/10.98)=7.33$, $p=.013$, Cz, $F(2.00/14.00)=13.16$, $p=.001$, and Pz, $F(2.00/14.00)=23.72$, $p<.001$. Inspection of the data shows that there was a uniform decrease in P300 amplitude as the stimulus

(both targets and non-targets) went from rare to frequent, however, the changes are more pronounced at the Cz and Pz leads. Differences held across stages, however, the 4-way interaction approached significance, $F(9.76/68.31)=1.58$, $p=.134$.

P300 Latency Figure 10 is a graph of P300 latency through the wake-sleep transition at different leads. P300 shows a large increase in latency from the awake conditions to the sleep conditions, and a general separation of latencies at the different leads during sleep. The analysis of variance supports this showing a Stage by Lead interaction, $F(8.00/56.00)=3.06$, $p=.006$. During the awake conditions and Stage 1, P300 latencies are relatively consistent across leads, and no effects are seen. At stages 2a and 2b however, P300 latency shows a significant effect for lead $F(2.00/14.00)=3.81$, $p=.048$, and $F(2.00/14.00)=7.25$, $p=.007$, respectively). Mean latencies at Fz, Cz, and Pz for Stage 2a were 471 ms, 461 ms, and 424 ms respectively, and for Stage 2b were 459 ms, 481 ms, and 452 ms. The main effect for stage was also significant, $F(4/28)=34.17$, $p<.001$, and post hoc tests indicated that while the increase in latency from Awake-Supine (335 ms) to Stage 1 (471 ms) was significant, Awake-Sitting (362 ms), Stage 2a (452 ms), and Stage 2b (464) were not significantly different from each other.

N200 Amplitude Figure 11 is a graph of N200 amplitude at different stages for each probability condition. It is apparent that, when subjects were awake during the P8 and the P2 conditions, target-nontarget differences were found with greater N200 amplitude to the more frequent of the two stimuli. When subjects were asleep, smaller N200 amplitudes were found for the more frequent of the two stimuli during sleep. In support of this, the analysis of variance yielded a Probability by Stimulus by Stage interaction, $F(4.37/30.58)=2.38$, $p=.069$, with the Probability by Stimulus effect significant at Awake-Supine, $F(1.84/12.888)=11.55$, $p=.002$, and Stage 2, $F(2.00/14.00)=4.26$, $p=.036$, but not at any other stage. At Awake-Supine, Stimulus was significant at the P8 condition, $F(1/7)=12.14$, $p=.01$, with targets showing greater amplitude than non-targets. Amplitudes were -2.26 μv and 0.19 μv respectively. At Stage 2a, the Stimulus effect was significant at the P8 condition, $F(1/7)=6.37$, $p=.040$, with non-targets showing greater amplitude than targets. Amplitudes were -10.02 μv and -5.51 v. respectively.

Figure 12 is a graph of N200 amplitude at different stages and stimulus type collapsed across leads. Probability had the same effect on target and non-target amplitude during the wake stages and the sleep stages. However, the effects during the sleep stages were opposite those during the awake stages. That is, N200 amplitude was higher when the eliciting stimulus was frequent during wakefulness but, during sleep, N200 amplitude was higher when the eliciting stimulus was rare. This held for all stages except Stage 2b, and an examination of the ERPs for Stage 2b shows an atypical negative prestimulus baseline shift in the target p=.2 and p=.5 waveforms which may explain the absence of any target differences for this stage. The analysis of variance

for Probability by Stimulus at Awake-Supine showed an effect for non-targets, $F(2.00/14.00)=6.18$, $p=.012$. Inspection of means indicates that N200 amplitude is greatest at the P2 condition ($p=.8$, -2.34 μv), followed by the P5 ($p=.5$, -1.06 μv) and P8 ($p=.2$, 0.19 μv) conditions, however post-hoc comparisons failed to reveal any differences. No probability effects were significant at stage 2a.

In all conditions, N200 shows a continuous increase in amplitude from the awake conditions through sleep Stage 2a, and a general decrease from Stage 2a to 2b. The main effect for stage was significant, $F(4/28)=5.87$, $p=.033$, however post-hoc tests indicate that there were no differences between any stages.

Figure 13 is a graph of N200 amplitude at different leads, for targets and non-targets grouped by probability level, shown for each stage. Lead effects are seen, N200 amplitude showing a frontal focus at Awake-Sitting and Awake-Supine, and a central focus throughout sleep. The two way Lead by Stage interaction was significant, $F(1.43/9.98)=4.28$, $p=.056$, showing a Lead effect for Awake-Sitting, $F(1.49/10.43)=22.61$, $p<.001$, and Awake-Supine, $F(1.26/8.83)=8.72$, $p=.013$. Mean amplitudes at Fz, Cz, and Pz, for stage Awake-Sitting were -1.26 μv, 2.00 μv, and 2.65 μv, and for Awake-Supine were -1.95 μv, -1.44 μv, and -0.13 μv, respectively. During the remaining 3 sleep stages, there were no effects for lead.

N200 Latency Figure 14 is a graph of N200 latency through the wake-sleep transition at different leads. N200 shows a large increase in latency from the awake conditions to the sleep conditions, and a general leveling of latency during sleep. The analysis of variance yielded a main effect for Stage $F(2.17/15.16)=22.06$, $p<.001$. Post-hoc tests indicated a significant increase between Awake-Sitting (255 ms) and Stage 1 (328 ms), but that Awake-Supine, (281 ms), Stage 2a, (332 ms), and Stage 2b, (333 ms) were not significantly different from each other.

Discussion

The primary purpose of the present study was to compare the effects of target probability on ERPs recorded during wake, sleep and the transition from wake to sleep to learn if the underlying processes responsible for ERP components in sleep are similar to the processes responsible for ERP components in wake. It was expected that for P300, probability effects and target-nontarget differences would be found at Awake-Sitting, replicating previous studies. Based on the results of one previous study, (Wesensten & Badia, 1988) it was hypothesized that these differences would persist in sleep. During sleep, P300 was expected to shift in latency, and N200 was expected to show a dramatic increase in amplitude.

The P300 Component

As expected, probability effects for P300 and RT were found at Awake-Sitting. Target P300 latency varied as a result of probability level, P300 showing a shorter latency for the P8 condition than for the P2 condition. RT also decreased from P2 to

P8, the change in RT with probability being almost twice that of the change in P300 latency (59 ms/33 ms). Duncan-Johnson and Donchin (1982) reported similar findings and concluded that the RT changes were due to both speeded stimulus evaluation and a change in response strategy with different probabilities, and that the changes in P300 latency were due to shorter stimulus evaluation, the response being emitted after a less complete evaluation of the stimulus.

Consistent with past studies, during both Awake-Sitting and Awake-Supine, P300 amplitude was found to be maximal over Pz (Donchin, et al. 1986). Probability effects were evident in P300 amplitude during both Awake-Sitting and Awake Supine, replicating the findings of previous studies of the effects of probability on P300 (Duncan-Johnson & Donchin, 1977; Squires, Wickens, Squires, & Donchin, 1976; Tueting, Sutton, & Zubin, 1971). P300 at Pz was largest to the rare tones and smallest to the frequent tones for both targets and non-targets. Thus at P2, the targets elicited greater amplitude P300s than the non-targets, and at P8, the non-targets elicited the greater amplitude P300s.

Task relevance effects were also present during Awake-Sitting. At the P5 condition where target and non-target probability levels were equal, P300 at Pz was significantly greater to targets than to non-targets. This larger amplitude to the more task relevant stimuli (targets) presumably reflects cognitive processing demands (Duncan-Johnson & Donchin, 1977; Squires, Wickens, Squires, & Donchin, 1976).

During the Wake-Sleep transition, probability and task-relevance effects on P300 amplitude disappeared during Stage 1 and 2a. During stage 2b, probability effects to targets, as well as task relevance effects (target-nontarget differences at P5) reappear. This indicates that the P300 recorded in stage 2b is characterized by the same functional relationship to experimental variables as the P300 recorded in wakefulness, and may be considered to represent the same underlying processes. The absence of probability and task relevance effects on P300 during Stage 1 and Stage 2a may be related to processes surrounding sleep onset, if sleep onset is seen as a gradual transition or period (Ogilvie & Wilkinson, 1988) encompassing both Stage 1 and portions of Stage 2 sleep. Attention may be diverted during this period by processes specific to sleep onset (hypnagogic phenomenon), but this is contradicted by the presence of responding in Stage 1 sleep. Another possibility is that P300 is attenuated by N200 during this period.

As expected, during Sleep, P300 showed a large increase in latency consistent with the findings of other studies (Buchsbaum, et al. 1975; Wesensten & Badia, 1988). Based on the persistence of probability and task relevance effects in stage 2 sleep, it is believed that this increase in latency reflects a lengthening of stimulus evaluation time (Bostock & Jarvis, 1970; Duncan-Johnson & Donchin, 1982; Wilkinson & Morlock, 1967), and not the emergence of a different process in sleep (Weitzman, et al. 1964). Stage 2 P300 latency differences between the present study

and the P300 reported in the Wesensten & Badia, (1988) study indicate that the P300 component found in this study is not the same as the P300 component reported in the Wesensten & Badia study. The P300 latencies for Stage 2 Sleep in the Wesensten & Badia (1988) study and the present study were 700 ms, and 460 ms respectively.

Response probability showed a continuous decline in sleep, with responding nearly absent ($p<.02$) in Stage 2 sleep. This is consistent with other studies (Ogilvie & Wilkinson, 1988). If the P300 in sleep reflects continued stimulus evaluation as this study indicates, the causes of decreased responding in sleep are more probably due to a decrease in the subject's ability or motivation to respond, than to a decrease in the ability to process information.

The results of this study indicate that the P300 of wakefulness and the P300 recorded after sleep onset are the same component, reflecting the same cognitive processes. These processes may be suspended or masked during sleep onset, but reappear once sleep is established.

The N200 Component

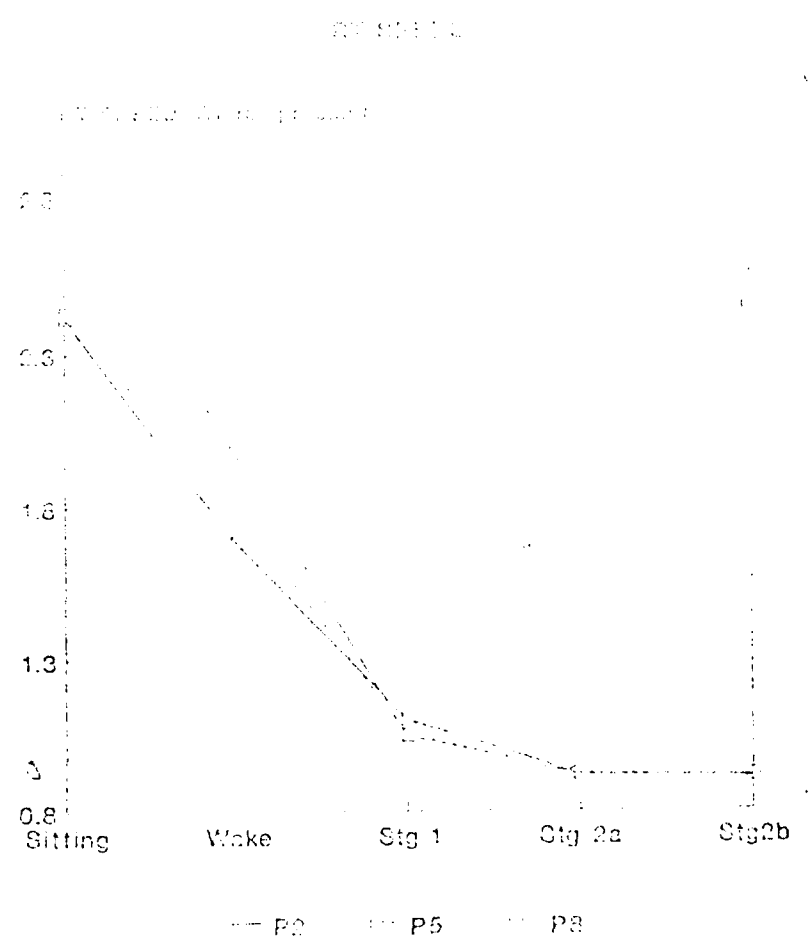
Consistent with prior research, the N200 component displayed an increase in amplitude (Buchsbaum, et al. 1975; Wilkinson, Morlock, & Williams, 1966) and latency (Wesensten and Badia, 1988) from the awake stages to the sleep stages. During sleep, N200 latencies were relatively stable compared to latencies in the awake stages. Although amplitude appeared to be dependent on probability, the rare tones eliciting the greater amplitude N200s, this was not statistically significant. Target-nontarget differences at the P8 condition in stage 2a, with the higher amplitude N200s being elicited by the rare non-targets, gives some support to this observation.

The effects of probability on the N200 recorded in the Awake-Supine condition are opposite those documented in previous studies (Naatanen & Picton, 1987; Ritter et al., 1983). That is, instead of N200 amplitude increasing as the tones became more rare, N200 amplitude increased as the tones became more frequent. An examination of the waveforms indicates that no N200 waveform is evident for many of the ERPs in wakefulness. This is consistent with previous studies (Simson, Vaughn, & Ritter, 1976) reporting that N200 is often obscured by other components when physical stimuli are present, as in a P300 paradigm. In the present study, when no scorable N200 waveform was present, the software scoring program recorded N200 amplitude during the beginning of the P300 deflection, and consequently when the P300 deflection is largest, the measured N200 was smallest. Thus, during the awake conditions N200 is often obscured by other components, and the probability effects reported earlier may be due to an artifact of P300.

In previous studies, (Wesensten and Badia, 1988), the increase in N200 amplitude during sleep has been attributed to a separation of the N200-P300 complex. In the present study, the relationship of N200 and P300 latencies remains relatively

stable. The increase in P300 latency during sleep was, on the average, 50 ms greater than the increase of N200 latency during sleep.

While replicating the results of previous studies showing an increase in N200 latency and amplitude during sleep. Data concerning the effects of probability on N200 during sleep are inconclusive. The results concerning N200 are not inconsistent with the tenet that the N200 of sleep is a reflection of the same processes as the N200 of wakefulness.



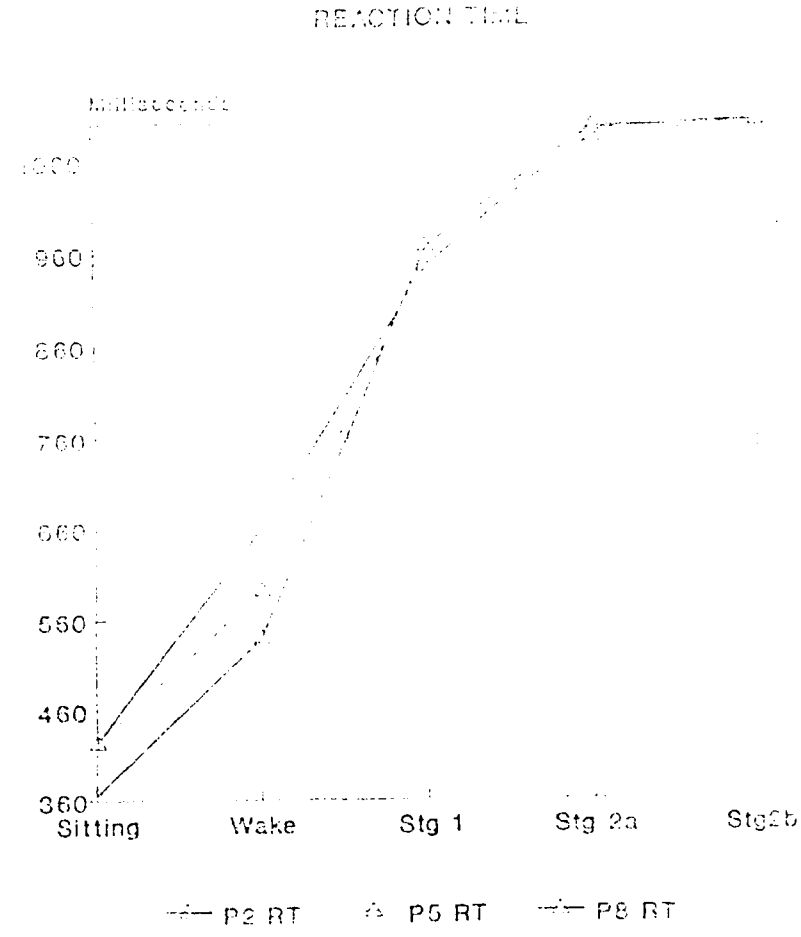


Figure 1 - Target Reaction Time Speed across Stages - Target Reaction Time across Stages

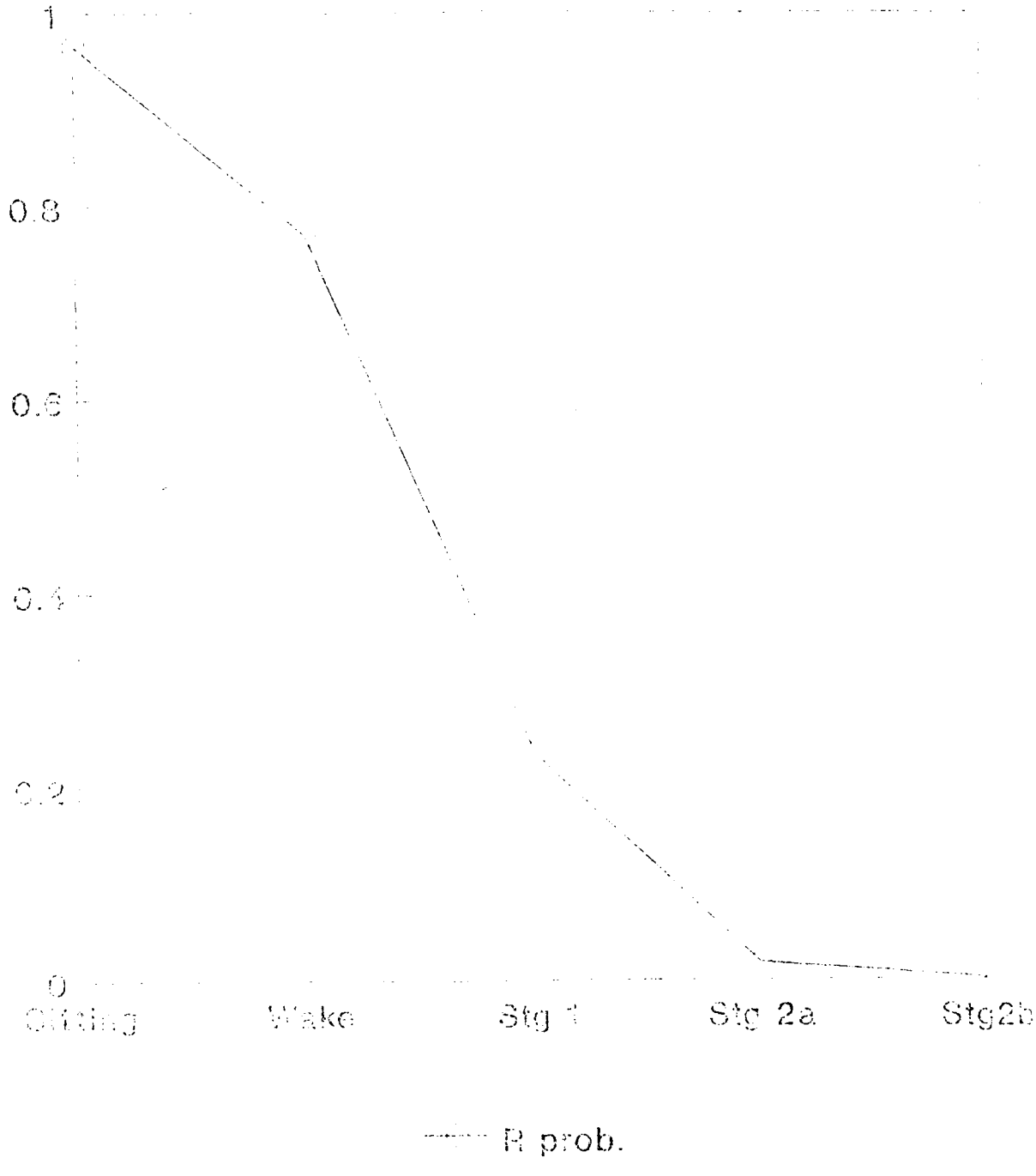


Figure 2 - Target Response Probability across Stages

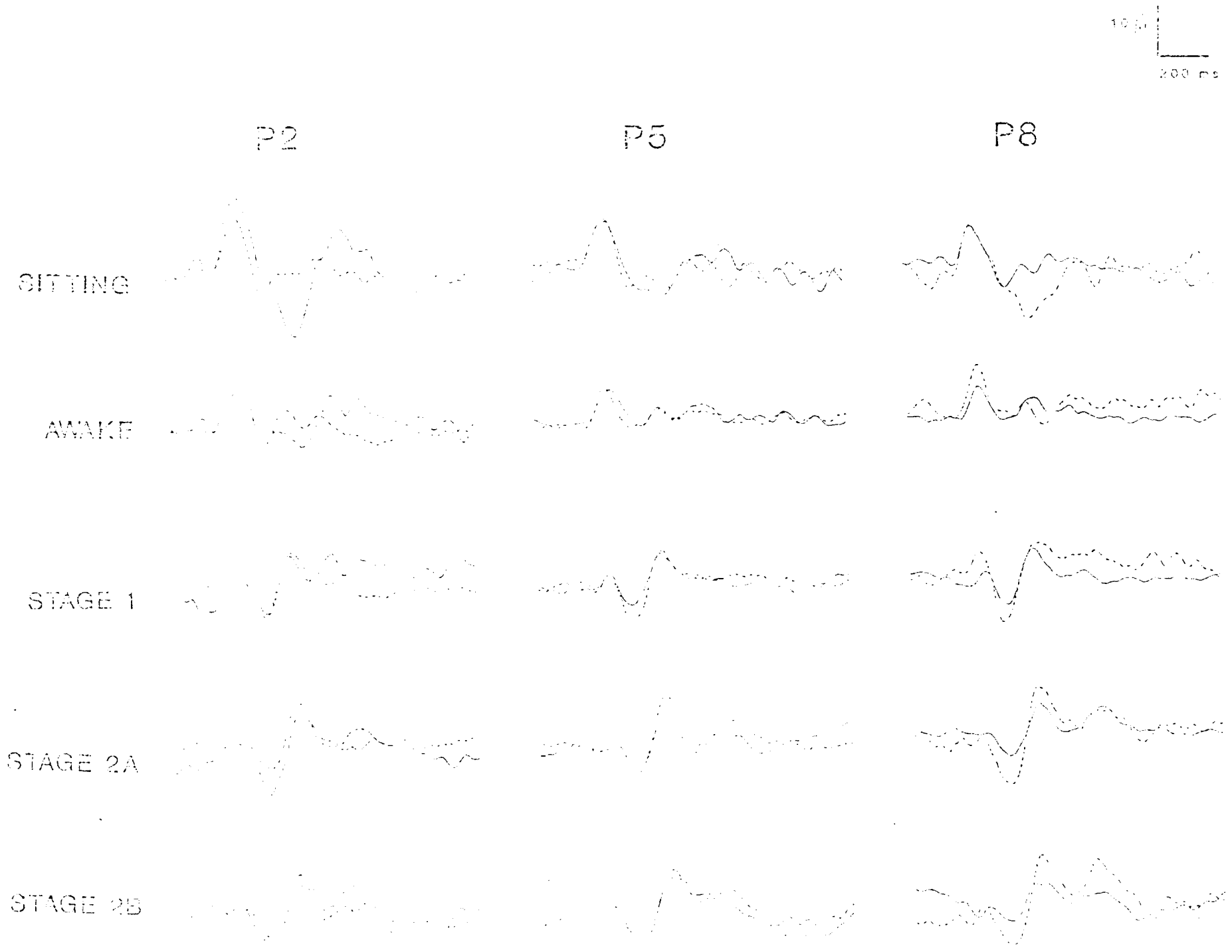


Figure 3 - Grand Averages Fz across Probability and Stages

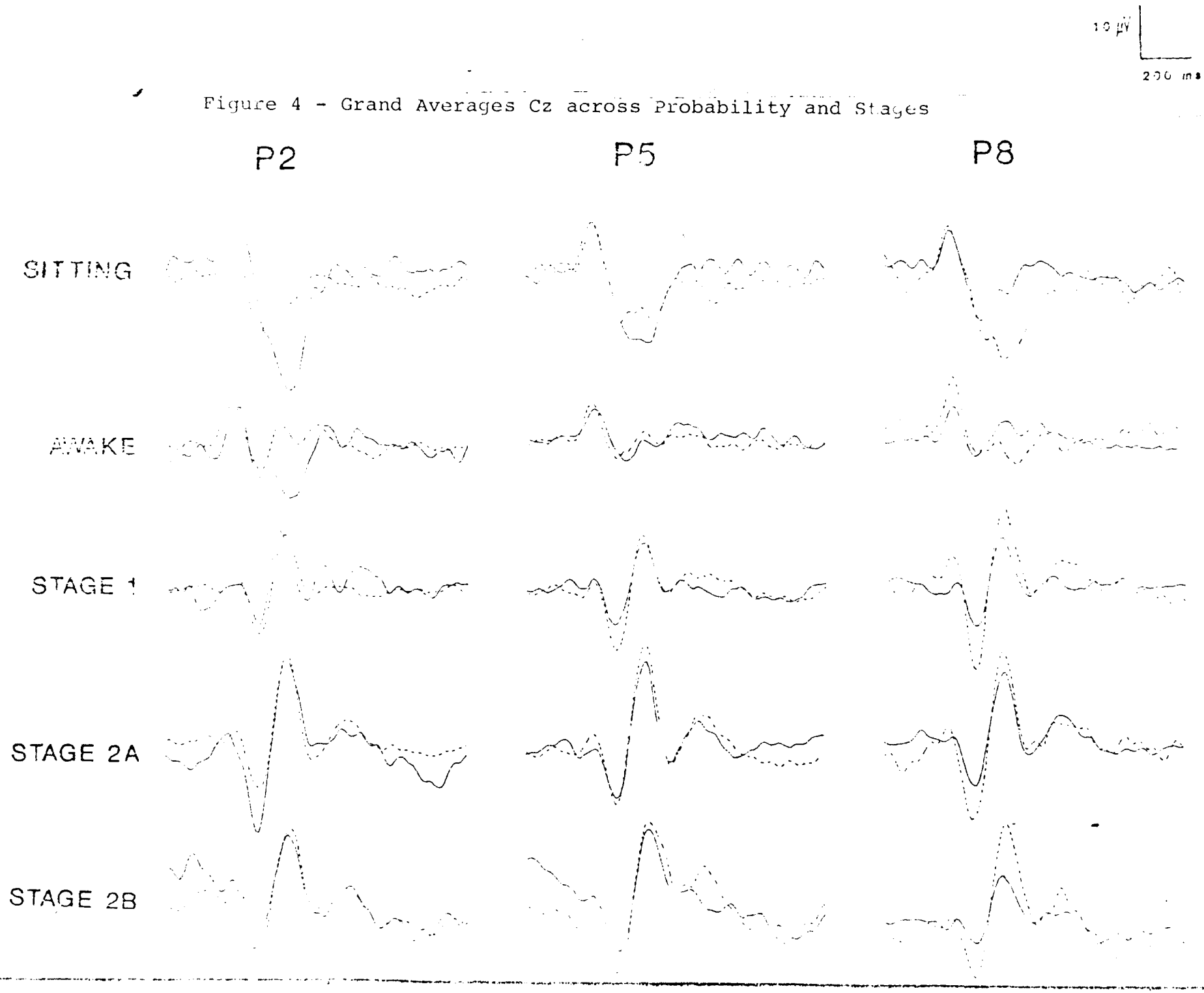
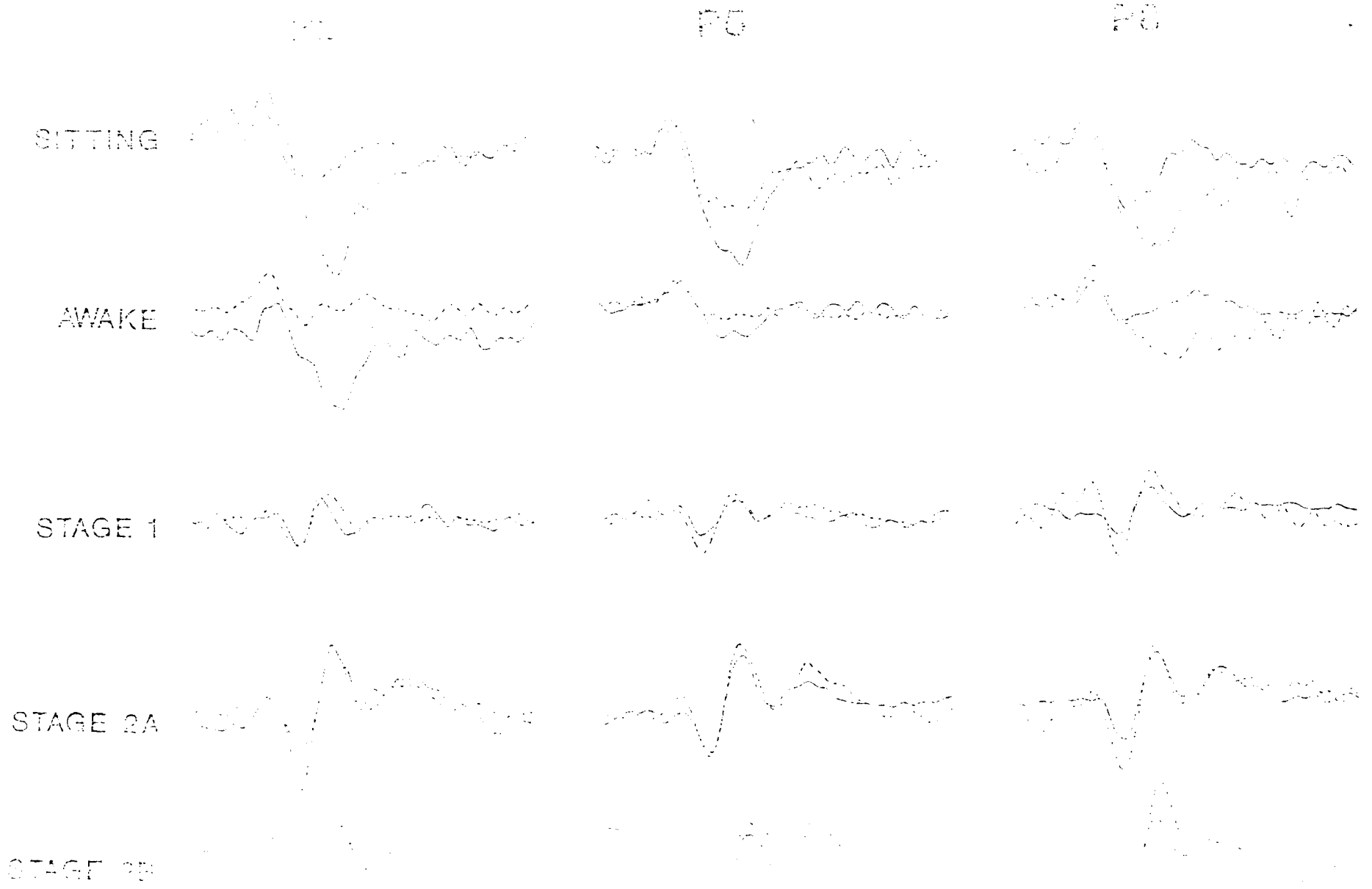


Figure 4 - Grand Averages Cz across Probability and Stages

Figure 5 - Grand Averages Pz across Probability and Stages



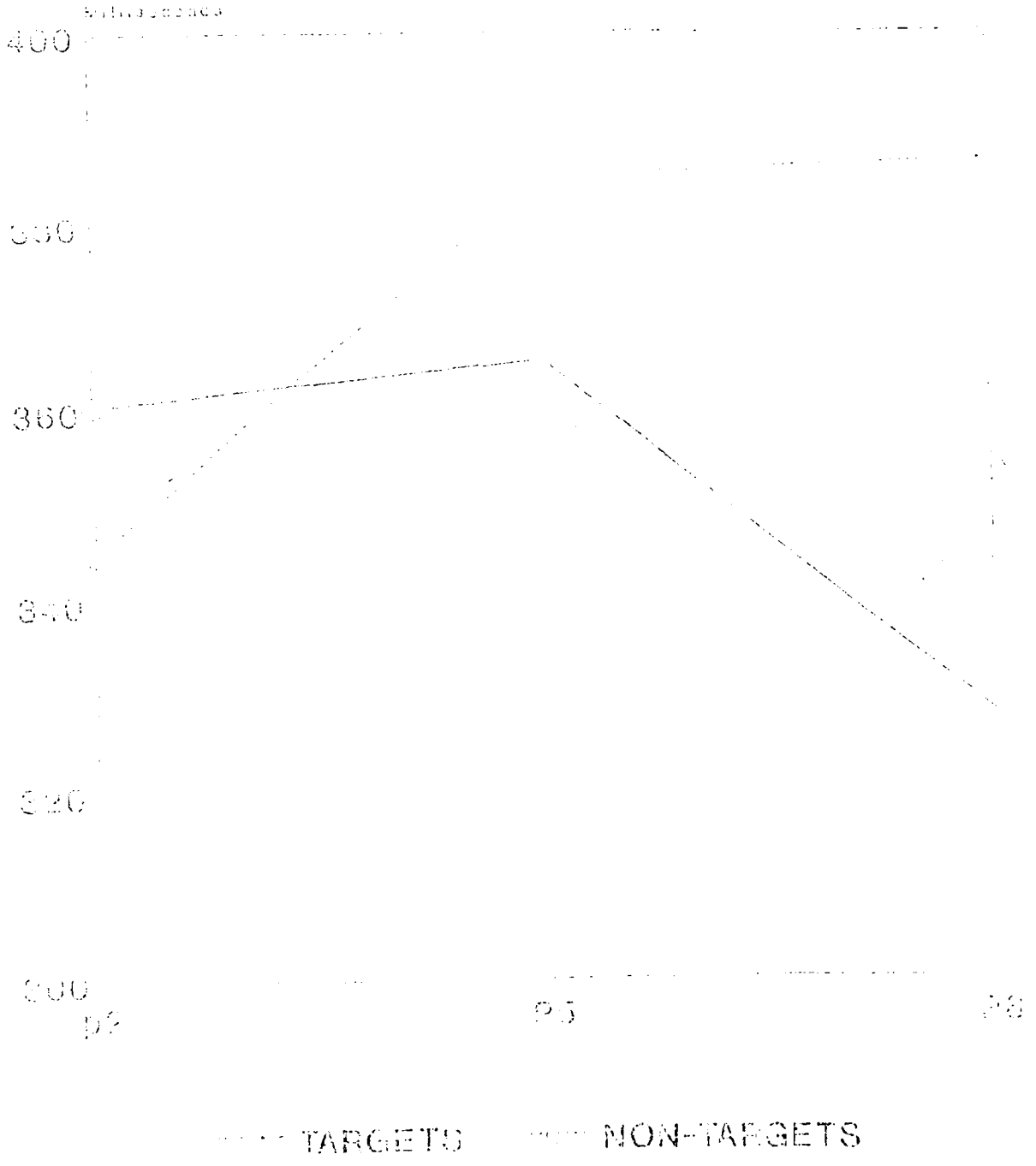


Figure 6 - Probability Effects on P3 Latency - Awake Sitting

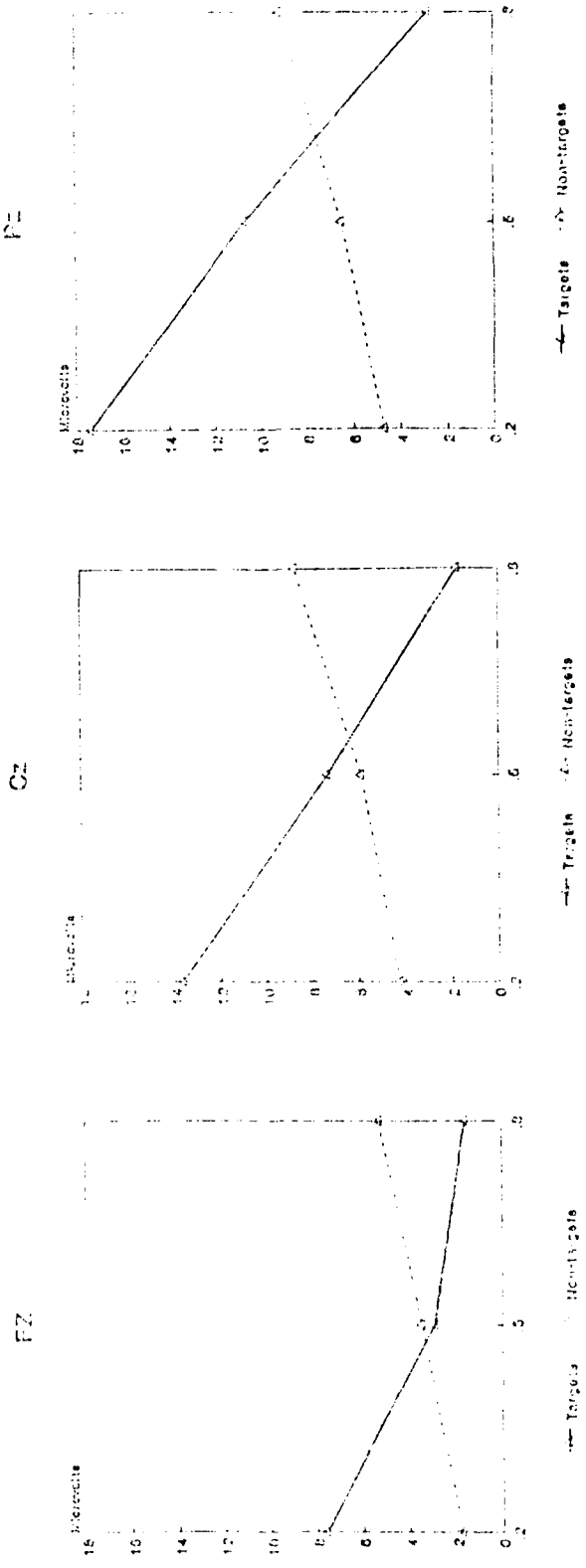


Figure 7 - Probability Effects on P3 Amplitude - Awake Sitting

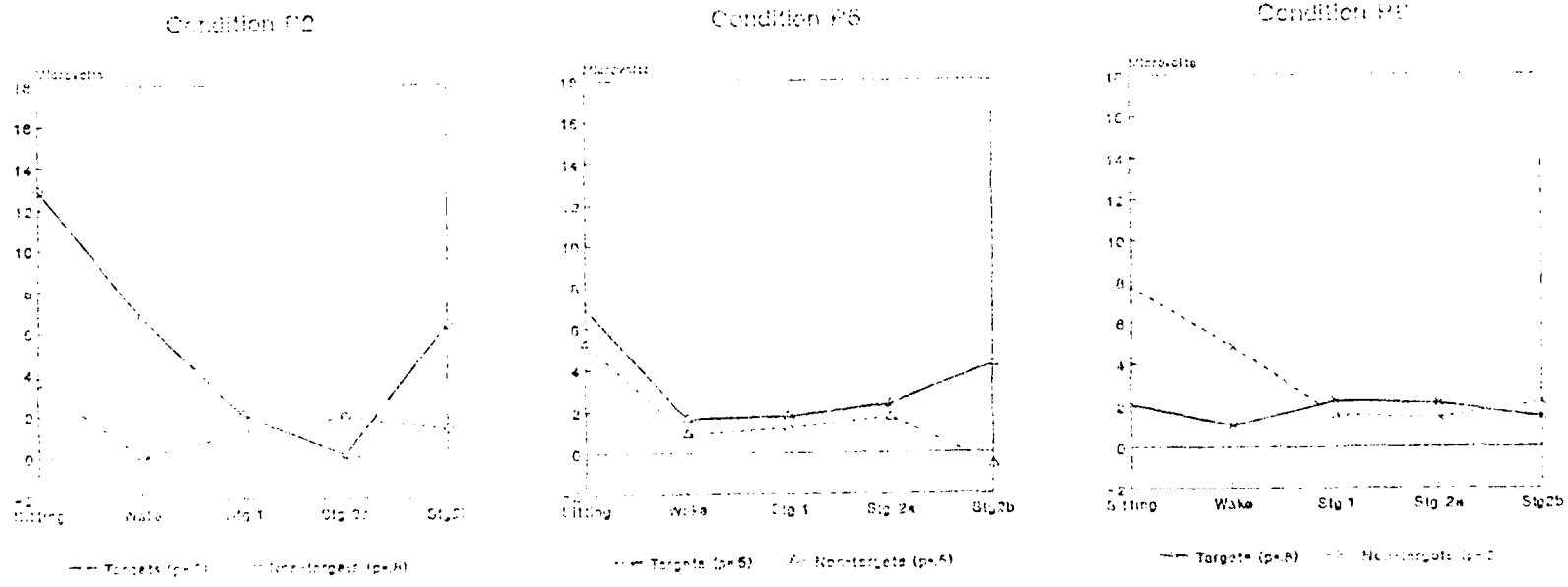
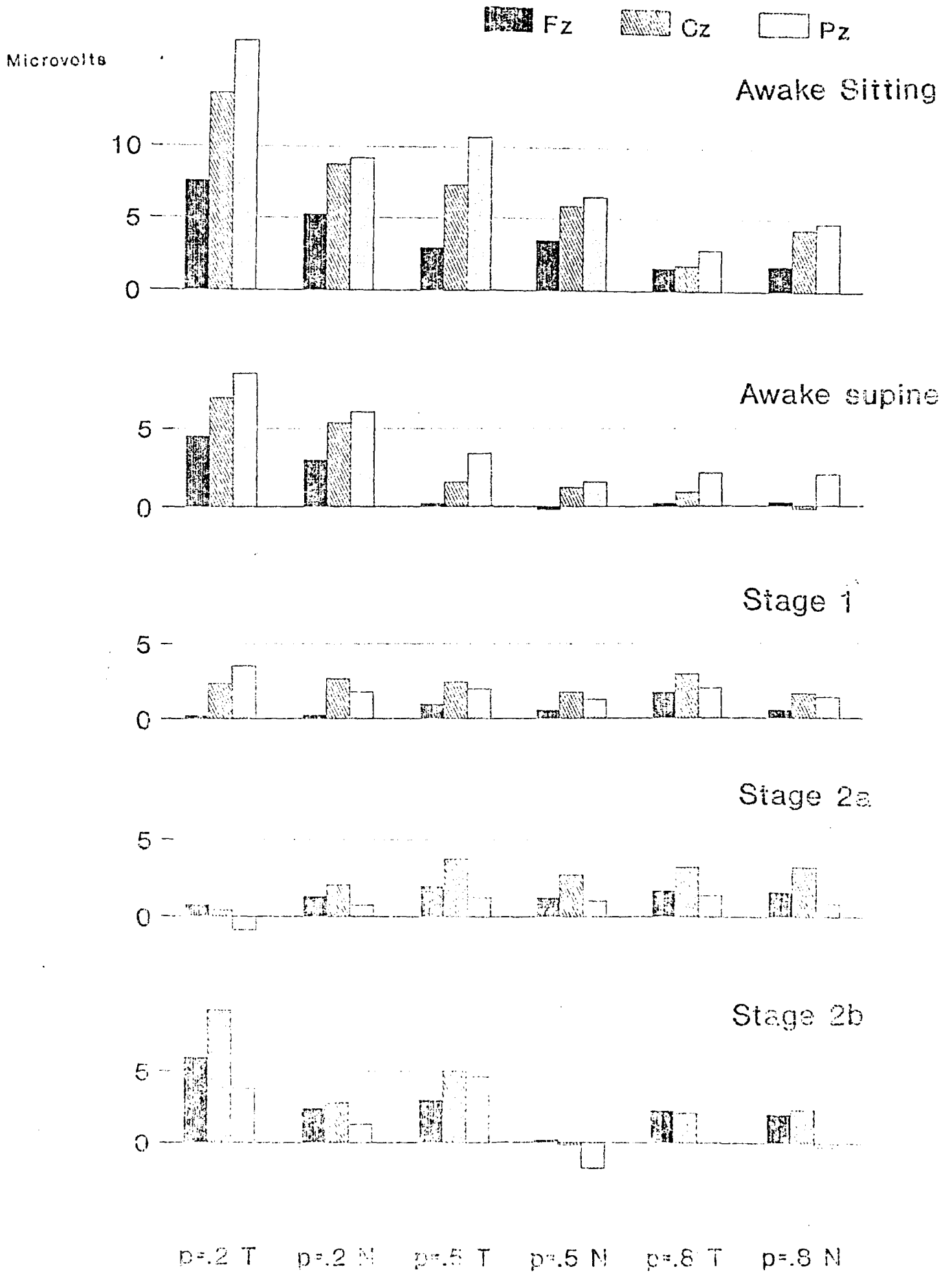


Figure 8 - P3 Amplitude Targets and Non-targets at Same Condition

Figure 9 P3 Amplitude Across Conditions and Stages



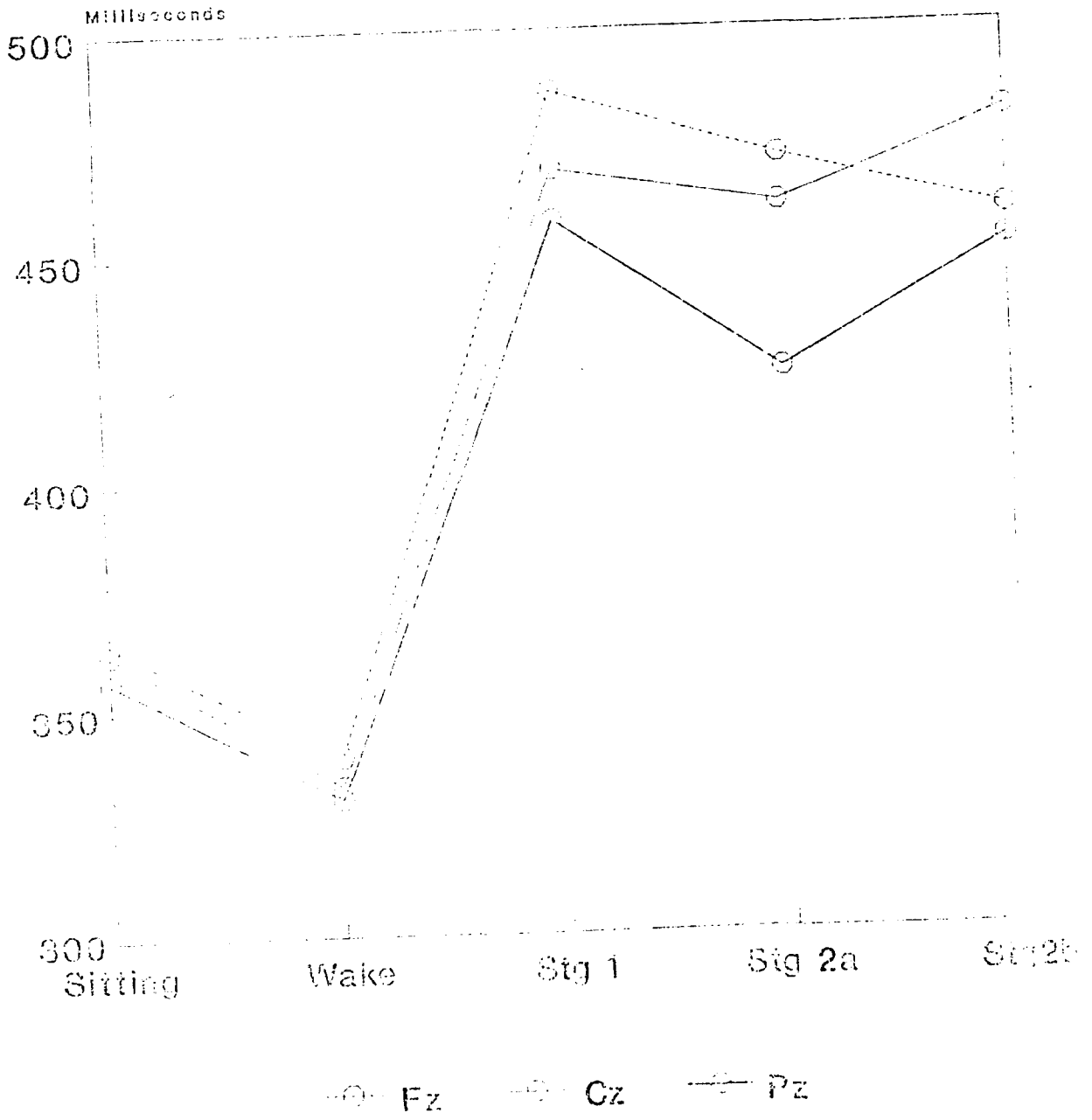


Figure 10 - P3 Latency During the Wake-Sleep Transition

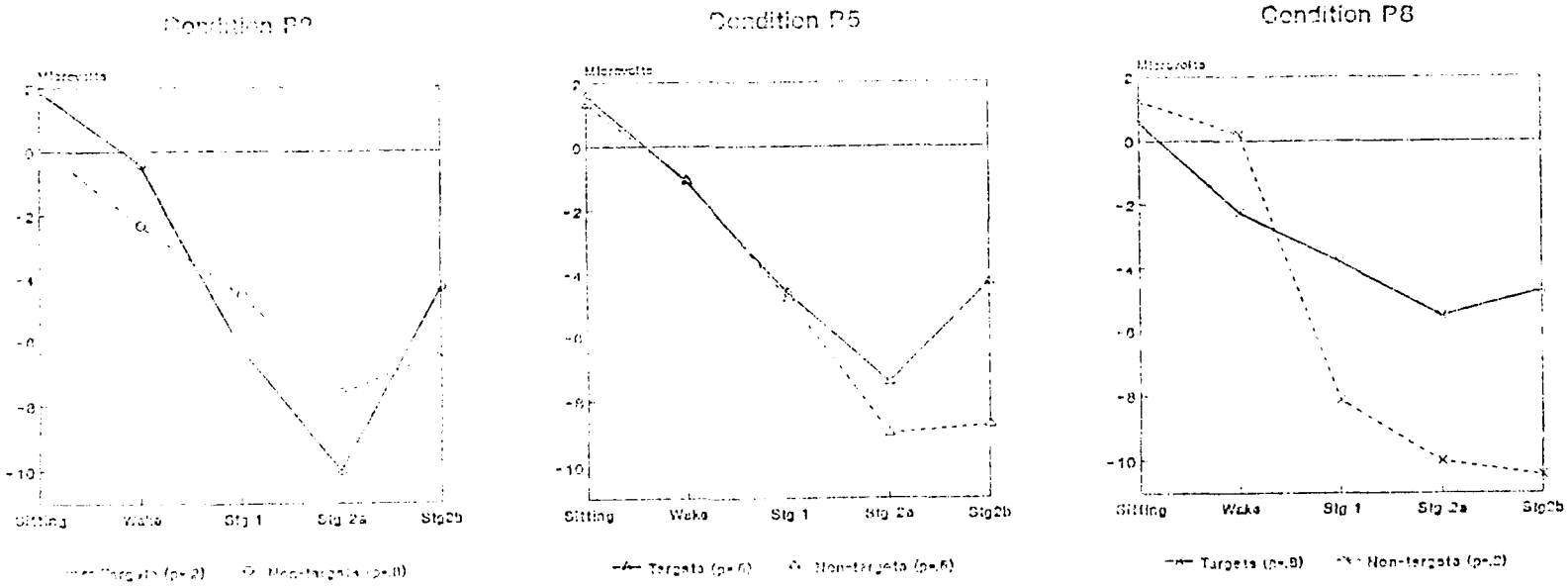


Figure 11 - Targets and Non-targets at Same Condition - N2 Amplitude

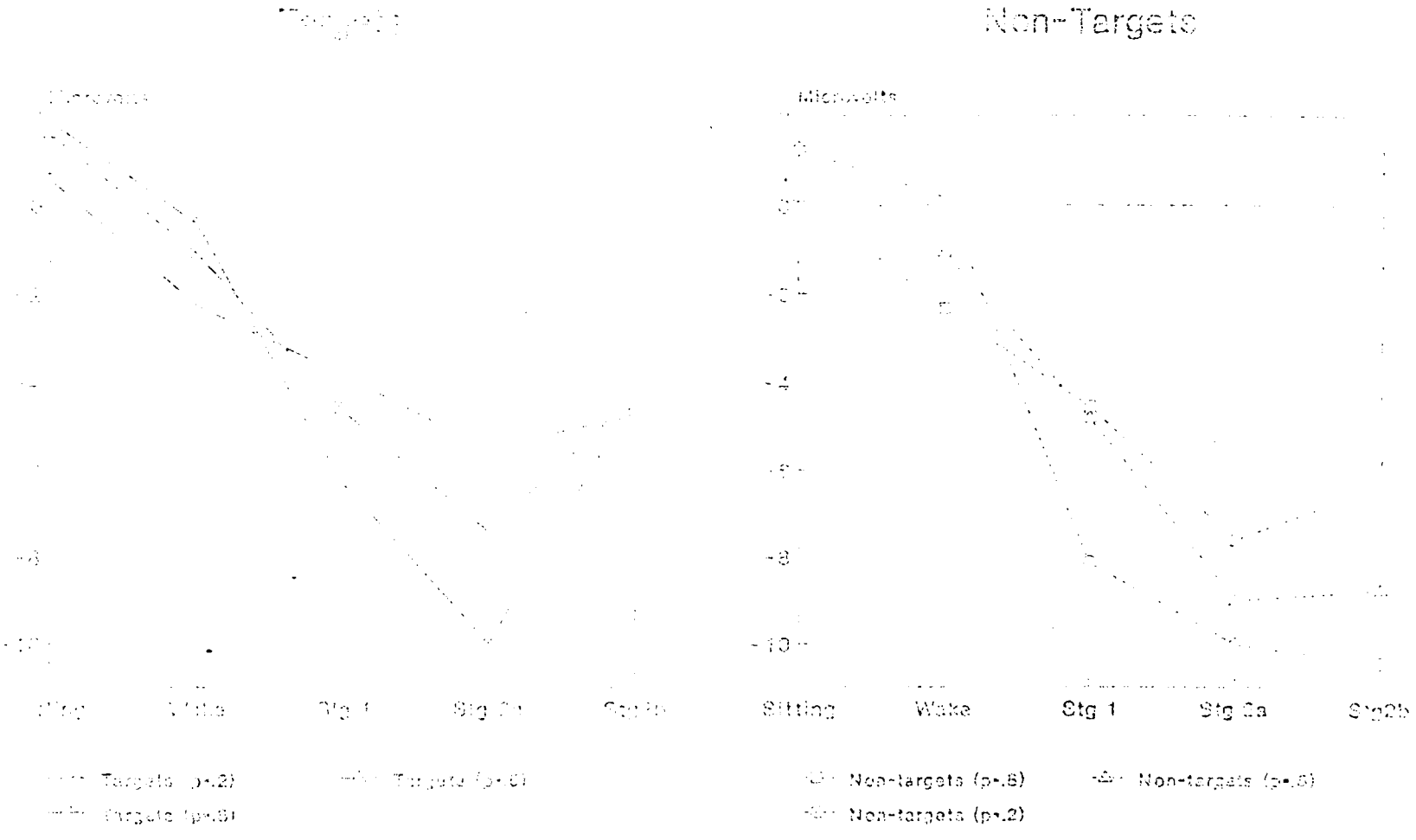
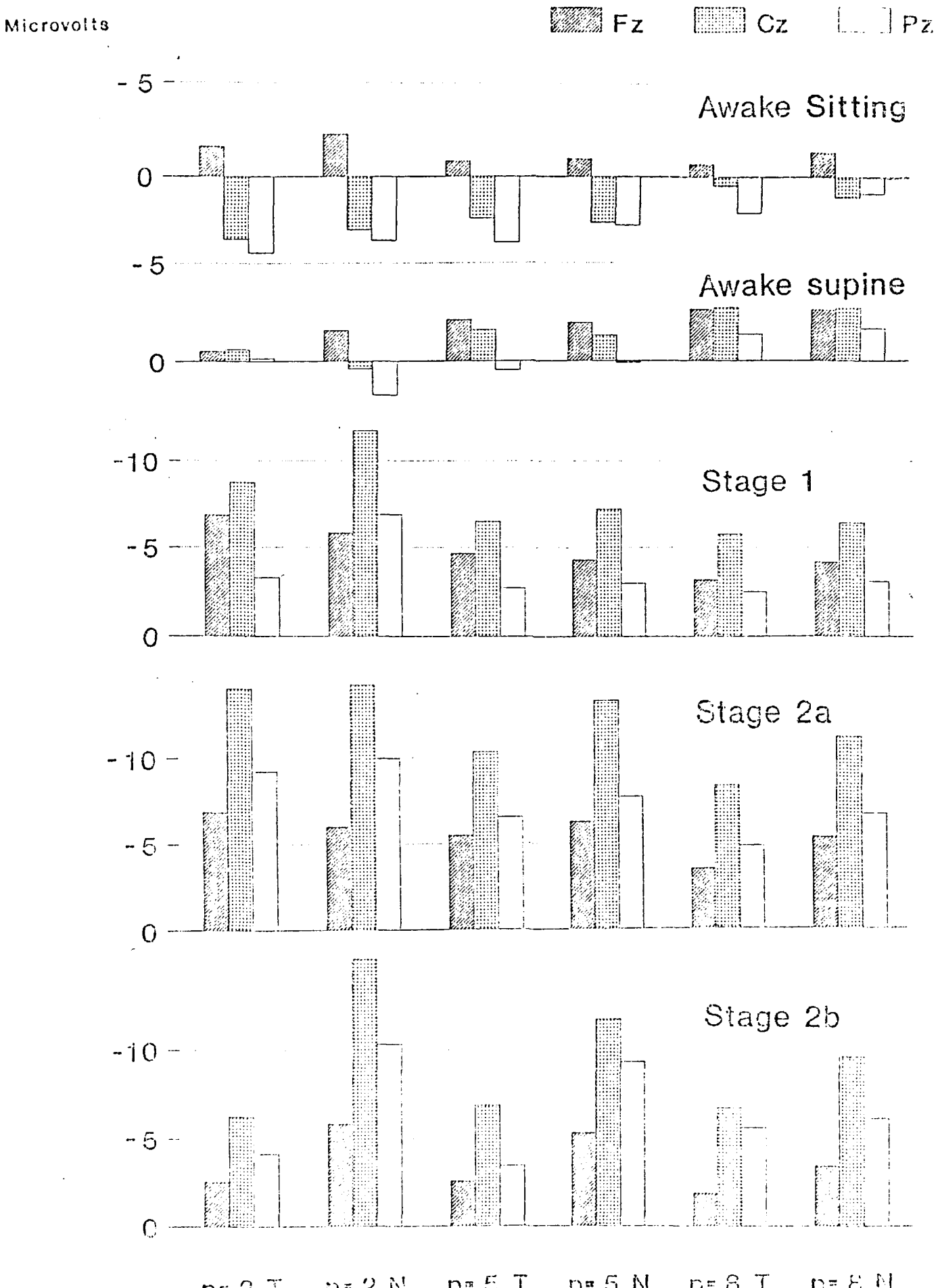


Figure 12 - N2 Amplitude During the Wake-Sleep Transition

Figure 13 N2 Amplitude Across Conditions and Stages



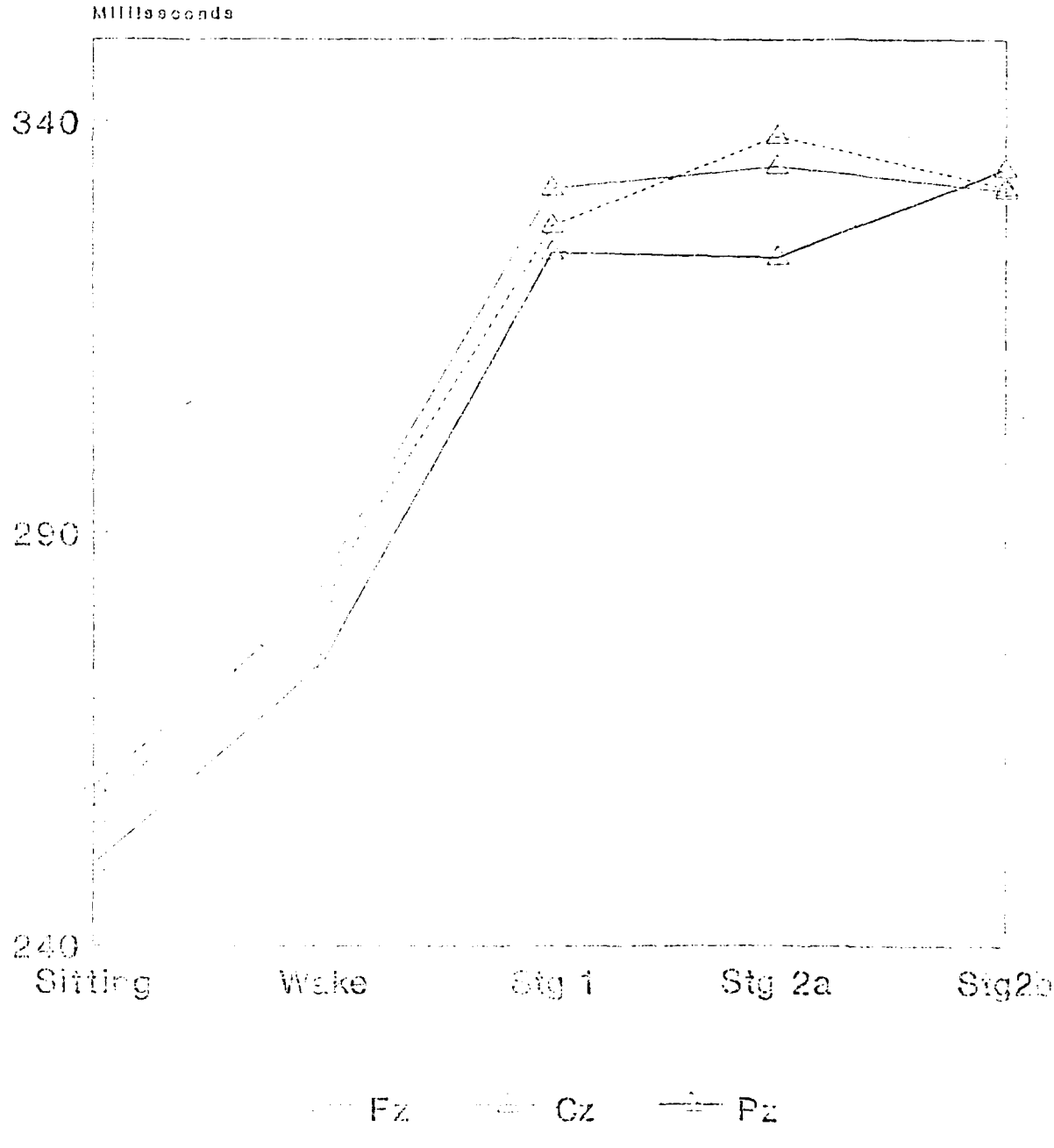


Figure 14 - N2 Latency During the Wake-Sleep Transition

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6.9 Experiment 9 - Bright Light Effects on Body Temperature, Alertness, EEG, and Behavior.

The following research deals with the effects on humans of exposure to bright or dim light during the nighttime hours. It focusses on the immediate psychophysiological and behavioral effects of photic stimulation rather than on circadian changes, e.g., phase shifts. However, since the research relates to body temperature and to melatonin release by the pineal gland, both of which are primary markers of circadian rhythms, the data should enhance our understanding of the circadian system.

The effects of bright light on the temperature trough and the melatonin onset period are well documented. Depending upon when human subjects are exposed to nighttime light of sufficient intensity and duration, both the temperature trough (e.g., Czeiler et al., 1989) and nighttime melatonin release by the pineal (e.g., Lewy & Sack, 1989; Lewy, Sack, & Singer, 1984) can be phase advanced or delayed (phase response curve). In addition to a phase response relationship, nighttime bright light (BL) exposure also has immediate effects. For example, when humans are exposed to BL during the melatonin release period (2100-0700 hrs), plasma melatonin levels begin to decrease within 10 to 20 minutes and, within an hour, daytime melatonin levels are reached (Lewy, Wehr, & Goodwin, 1980). Up to a point, the brighter the light, the greater the melatonin decrease (McIntyre, Norman, Burrows, & Armstrong, 1989). If subjects are then placed under dim light (DL), melatonin levels are restored to normal nighttime values within about 40 minutes (Lewy et al., 1980). Controlling nighttime levels of melatonin may be useful since several studies have suggested that melatonin has hypnotic properties. For example, melatonin administered orally at night induces drowsiness and has a beneficial (enhancing) effect on various sleep measures [e.g., (Arendt, 1988; Waldhauser, Saletu, & Trinchard-Lugan, 1990). Similarly, daytime ingestion of melatonin results in reports of sleepiness, fatigue and in performance decrements (Leiberman, Waldhauser, Garfeild, Lynch, & Wurtman, 1984).

The above findings suggest that the nighttime decrements in alertness and performance observed under sleep deprivation may be due, in part, to melatonin release. If so, it may be possible to attenuate these nighttime decrements by exposure to light intensities known to suppress melatonin synthesis. Thus, exposure to bright lights during nighttime hours should enhance alertness and performance through the suppression of melatonin release, or if already released, through its depletion. In contrast, exposure to dim light during the nighttime hours should diminish alertness since melatonin release is not suppressed. In short, measures of alertness should be enhanced under bright light stimulation and diminished under dim light. Therefore, one question we addressed is whether alertness and performance levels vary as a function of bright and dim light exposure. Specifically we asked "Will nighttime exposure to light intensities sufficient to suppress

melatonin synthesis reduce sleepiness and enhance nighttime alertness and performance levels during sustained wakefulness?" We should note at the outset that we did not assay melatonin levels but, instead, used a light intensity found repeatedly to suppress nighttime melatonin to near daytime levels (Bojkowski, et al., 1987; Lewy et al., 1980; McIntrye et al., 1989). A second question relates to nighttime body temperature. There is some suggestion that the pineal and melatonin may be involved in thermoregulation in animals (Heldmaier & Hoffman, 1974; Heldmaier, Steinlechner, Rafael, & Vsiansky, 1981; Ralf, Firth, Gern, & Owens, 1979). For example, there is also evidence in animals suggesting that injection of melatonin or pinealectomy affects body temperature [see Ralf et al. for a review]. Further, in humans, body temperature and melatonin levels appear to be inversely related in that the nocturnal "window" of melatonin release corresponds to the nocturnal "window" of lower body temperature. Given such a relationship, it may be possible to gain relatively immediate control over nighttime levels of body temperature by using an intensity of photic stimulation known to deplete melatonin levels. Specifically we asked "Will exposure to bright or dim light result in relatively immediate increases or decreases in nighttime body temperature?"

The questions noted above were addressed using two different procedures. With one procedure subjects were given 90 minute blocks of alternating bright and dim light across the nighttime hours while they remained awake. With the other, subjects were given either continuous bright or continuous dim light across the nighttime hours also while they remained awake. In addition, a daytime control condition was tested to determine whether bright and dim light during the daytime hours would exert an effect. Measures of body temperature, alertness, sleepiness and performance were recorded for all subjects.

Method

Subjects Forty four male students ranging in age from 18 to 32 years participated in the study. Females were not used because their body temperature rhythm is affected by the phase of their menstrual cycle. Subjects were screened and those with atypical sleep/wake patterns, sleep complaints, illness, or on medication were eliminated. Subjects were paid for their participation.

Design Four experimental conditions were tested each with a different group of subjects: 1) nighttime alternating BL-DL condition, 2) daytime alternating BL-DL condition, 3) nighttime continuous BL and 4) nighttime continuous DL condition. Subjects in the nighttime alternating condition (N=16) received 90 min blocks of bright light (5K lux to 10K lux) alternating with 90 min blocks of dim light (50 lux). Half of these subjects started with a 90 min BL block, the other with a 90 min DL block. Subjects in the daytime alternating condition (N=8) served as control subjects to assess the effects of daytime BL and DL exposure. They received two 90 min blocks of alternating BL and DL beginning at 1300 hrs. Half of them received BL first, the others DL first. Subjects in the nighttime continuous light

condition (N=19) were randomly assigned to either continuous nighttime BL (5K to 10 K lux; N=10) or continuous nighttime DL (50 lux; N=9). Light conditions for the latter subjects did not change at any time throughout the night and the testing period was divided into blocks similar to the alternating condition.

Apparatus Fluorescent light sources (40-watt cool white lamps) were used to obtain a light intensity of 5K to 10K lux (depending upon movement of subject). The lights were placed in front of subjects with an approximate distance of 46 cm from the center of the light bank to the subject's face. Beckman silver-silver chloride electrodes were used to record EEG (Fz, Cz, Pz; mastoid reference), EOG, EMG, ECG, and skin resistance levels. All physiological measures were recorded using a Grass Model 78D polygraph and digitized using a Data Translation (DT- 2821) A/D board, DT-Notebook (Signal Technologies, Inc.), and a Compaq 386/16 Deskpro computer. All channels were digitized at 200 Hz/s.

Measures for Analysis

Temperature. Body temperature was obtained using a FirstTemp tympanic probe (Intelligent Medical Systems, Model 2000A).

Behavioral Tasks. Performance was assessed for each block using several computer tasks selected from the Performance Assessment Battery (PAB) developed by Thorne, Genser, Sing, and Hegge (1985) and from those developed from the Bowling Green State University Psychophysiology and Sleep Research Laboratory. These included digit recall, logical reasoning, two-letter search, two-column addition, serial addition-subtraction, and a continuous performance task. To prevent glare on the computer monitor a polaroid screen was used. Also a hood was used consisting of a particle board and a draped black cloth that extended 38 cm in front of the monitor.

EEG Spectral Power and Dominant Frequency Analysis. A 2-min sample of EEG data (Fz, Cz, Pz) was collected while subjects sat quietly with their eyes open and focussed on a red dot on the wall in front of them. For each block spectral analysis of each subject's data was performed which yielded an amplitude power spectrum of the EEG frequencies between 0.5 Hz and 30 Hz in 0.5 Hz band widths. The latter also permitted an analysis of the dominant frequency for the theta (4- 7 Hz), alpha (8-12 Hz) and beta (15-30 Hz) bands.

Sleepiness. A maintenance of wakefulness test (Mitler, Gujavarty, & Browman 1982) was administered to assess sleepiness (alertness) for subjects in the continuous light condition. At the end of each block subjects remained seated upright as usual and were instructed to sit quietly but to try and remain awake. Testing of wakefulness was terminated following either three successive 30 sec epochs of stage-1 sleep, one epoch of stage 2 sleep, or after 15-min of wakefulness.

Procedures Subjects reported to the laboratory and practiced the performance tasks several times to ensure asymptotic levels of performance prior to the beginning the experiment. Those in the alternating light condition reported to the laboratory at 2100 and were given additional practice with the tasks till 2300.

At 2300 electrodes were attached and at 2400 the actual study began. Subjects remained awake (except for tests of sleepiness) until 0900 hours the following morning. Those receiving continuous bright or dim light were treated in a similar manner. The procedure consisted of a 9-hr modified constant routine procedure (Czeiler et al., 1985; Mills, Minors, & Waterhouse, 1978) that was divided into six 90-min blocks of alternating bright light (5K to 10K lux) and dim light (50 lux). The order of the light conditions (BL or DL first) was counterbalanced across subjects. Subjects tested during the daytime hours were given similar treatment prior to and during their two testing blocks. All subjects remained seated in an upright position for the entire study. Food and water intake were divided into equal portions and administered at the beginning of each defined block. Temperature was recorded every 30 min and a fixed order of testing was followed for each block, i.e., temperature #1, free-time, snack, temperature #2, first set of performance tasks, temperature #3, EEG recording for spectral analysis, MWT, and temperature #4.

Results

Data were analyzed with Analysis of Variance (ANOVA) for repeated measures with a Greenhouse-Geisser degree of freedom correction when appropriate.

Temperature

Alternating Nighttime Condition. Figure 1 shows temperature changes across the entire night for each of the alternating blocks of BL and DL. As noted, for some subjects (N=8) the starting light condition on Block 1 was BL; for others (N=8) the starting light condition was DL. However, 2 x 6 x 4 ANOVA (Order x Time-of-Night x Time within Block) revealed that the Order effect was not significant, $p > .05$, thus Order was omitted from subsequent analyses.

Several observations are apparent for both subgroups. First the typical circadian drop in temperature occurs early in the night and then later begins to rise in the early morning. An apparent trough occurs between 0500 and 0600 hrs (Blocks 4 & 5). Statistical analyses (2 x 3 x 4 [Light Condition x Time-of-Night x Time Within Block] ANOVA) indicated that this time-of-night effect was significant, $F(2,30)=9.8$ $p<.005$. However, the most interesting observation is the pattern of temperature changes under each light condition. Figure 1 reveals that increases and decreases in light intensity generally resulted in increases and decreases in body temperature. For both groups, when exposed to the DL, overall temperature within the block dropped. In contrast, when exposed to the BL, overall body temperature within the block increased or maintained except for Block 1 of the group given BL first. This observation was confirmed by a significant Light Condition x Time Within Block interaction, F (3.45) = 5.6, $p < .005$. We should note that the described light effects were seen in each of the 16 subjects.

Figure 2 shows the effects of bright and dim light using difference scores. The scores reflect the difference in

temperature at the beginning of the 90-minute compared to readings taken 30, 60, and 90 minutes later. The difference scores noted in Figure 2 are collapsed across order and blocks. As shown, under the DL condition, temperature dropped across the 90 min period; under the BL condition, temperature increased for the first two time periods, then maintained. Interestingly, the changes in temperature were usually apparent within 30 min. Statistical analyses support the above observations. The main effects of Light Condition (BL, DL) and Time Within Block (00, 60, 90 min) within a condition were significant, $F(1,15)=66.5$, $p<.0001$ and $F(3,45) = 5.6$, $p< .005$ respectively. The interaction of Light Condition and Time Within Block was also significant $F(3,45) = 29.8$, $p< .0001$. The BL and DL condition (Figure 2) differed at all time points beyond the first.

Daytime Control Condition. Figure 3 depicts body temperature under bright and dim photic stimulation for daytime subjects. The figure reveals no systematic effects of bright and dim light during the daytime hours. Statistical analysis (2 x 4 [Light Condition x Time Within Block] ANOVA) indicated that no main effect or interaction was significant, $p >.05$.

Continuous BL - DL Condition. Figure 4 depicts body temperature across the night for those subjects receiving continuous nighttime bright or dim light. As seen, a decrement in body temperature with an apparent trough between 0500 and 0600 hours occurred for both groups. Temperature data were analyzed with Light Condition x Time-of-Night ANOVA which indicated a significant Time-of-Night effect, $F(20,340) = 25.5$, $p < .005$. In addition, the BL condition tended to maintain temperature higher throughout the nighttime hours than did the DL condition, $F(1,17) = 9.2$, $p = <.01$. As shown in Figure 4, while temperature under the DL started out slightly higher than under BL, the decrement in temperature across blocks was considerably greater under DL. For the DL condition the drop in temperature across the night was about .6 degrees C and for the BL condition it was less than .3 degrees C. This Light Condition x Time of Night interaction was significant, $F(20,340) = 3.8$, $p <.05$.

EEG Spectral Power and Dominant Frequency

Alternating Condition-Spectral Power. There were marked differences in log power density between the BL and DL conditions for the beta band but not for the alpha and theta bands. Further, within the beta band the differences were most marked at the Cz scalp site. Figure 5a shows the pattern of activity at Cz for log power density contributed by the beta band. The log power density of beta under BL (M = 4.8) was greater than under DL (M = 4.4). The latter suggests that the BL condition was more alerting or arousing. As with temperature, increases and decreases in light intensity resulted in increases and decreases in log power density of beta. This difference was confirmed by 2 x 3 (Light Condition x Time-of-Night) ANOVA, $F (1,14) = 10.4$, $p < .001$. The Time-of-Night effect and interaction were not significant. In contrast to beta, there was a significant increase across blocks for log power density of theta, $F(2,28) = 5.9$, $p <.05$. The latter

increase most likely reflects increased sleepiness due to sustained wakefulness.

Dominant Frequency. The dominant frequency within the alpha, beta, and theta bands was also analyzed in a similar manner. The BL and DL condition had an effect on the dominant frequency within both the theta and beta bands but not the alpha band. The dominant frequency of beta under the BL condition was 19 Hz (Figure 5b), while under the DL condition it was 16 Hz, F (1,14) = 38.0, p <.0001. For theta, under BL the dominant frequency was 4.9 Hz; under DL the dominant frequency was 5.4 Hz, $F(1,14)$ = 13.1, p < .005.

Daytime Control Condition. Although the BL and DL daytime differences in log power density and dominant frequency were similar to the differences found during nighttime, none of the differences were significant for any of the EEG bands (alpha, beta, theta) at any of the scalp sites.

Sleepiness (MWT) under Continuous BL - DL Conditions

Sleep latency scores derived from the Maintenance of Wakefulness test were analyzed for the two groups exposed to continuous BL and DL. Figure 6 shows the changes in sleepiness that occur for these groups across the sleep deprivation period. As shown, differences in sleepiness were small for the first two blocks of continuous bright or dim light. However, the sleep latencies diverged sharply for the remainder of the night (Blocks 3, 4, and 5). By the last block subjects under the DL condition displayed sleepiness scores (M=4.3 min) that meet the requirements of pathological sleepiness. In contrast, under the BL, sleepiness scores (M=11.1) were similar to those found in normals during the daytime hours (25). Statistical analysis (2 x 5 [Light Condition x Time-of-Night] ANOVA) confirmed the existence of differences in sleepiness between the two light conditions, $F(1,17)$ = 12.8, p< .005 and that the difference increased as the night progressed; the interaction was significant, $F(4,68)$ = 4.4, p < .01.

Performance Measures

Alternating Condition. Performance measures were assessed by 2 x 3 (Light Condition x Time-of-Night) ANOVA and indicated that performance under BL tended to be better on all tasks and significantly so for Digit Recall [$F(1,15)$ = 4.7, p <.05), Two Letter Search [$F(1,15)$ = 5.3, p <.05] and Serial Add/Sub [$F(1,15)$ = 5.9, p <.05]. Performance under the DL condition was not significantly better on any task. All tasks tended to show a time-of-night deterioration.

Daytime Control Condition. In contrast to the better nighttime performance under the BL condition, performance during the daytime hours tended to be slightly, but not significantly, worse under BL. Continuous BL - DL Condition. As with the alternating condition, performance under the continuous light condition tended to be superior under BL for each task. When performance was analyzed across the six tasks over the five blocks by 2 x 5 (Light Condition x Time-of-Night) ANOVA, performance under the BL was better than under the DL 78% of the

time. However, the differences between the BL and DL condition did not reach significance, $p > .05$.

Discussion

The following is a summary of the results. For the nighttime alternating light condition, body temperature generally maintained or increased when subjects were exposed to BL and decreased toward normal values when they were exposed to DL. For the nighttime continuous light condition, body temperature dropped only slightly across the night under BL but dropped sharply under DL. There was no effect of BL and DL on body temperature for the daytime control subjects. Sleepiness was considerably greater under the continuous DL condition with the differences especially marked the latter part of the night. Nighttime performance on tasks generally was better under BL than under DL; this relationship was not found for daytime performance. Finally, alertness (EEG beta activity) was greater under BL than under DL during the nighttime hours but not during the daytime hours.

Others have shown that light exerts a powerful influence on the circadian (phasic) organization of our physiology and behavior (e.g., Czeiler et al., 1989; Lewy, Sack, Miller, & Hoban, 1987). Our data reveal that it also exerts powerful, immediate (tonic) effects on physiology and behavior. Whether the phasic effects reported by others and tonic effects reported here involve similar mechanisms or involve independent mechanisms remains an important question.

Also of interest to the present study was the relationship between nighttime body temperature and photic stimulation. Our data strikingly demonstrate that nighttime temperature varies systematically with bright and dim photic stimulation. Interestingly, the time period required to observe a change in body temperature due to light is similar to the time period required to observe a change in melatonin levels due to light. Thus, it could be that melatonin plays some role in the thermoregulation process.

Our findings are also relevant to those interested in the endogenous temperature rhythm unobscured by exogenous masking factors, such as sleep-wake rhythm, activity level, food intake (e.g., Folkard, 1989; Minors & Waterhouse, 1989). Investigators interested in the endogenous rhythm record temperature under awake conditions to remove the masking effect of sleep, use a constant routine procedure to remove the masking effect of activity, and provide aliquots of food to remove the masking effects of food intake. Our data suggest that ambient light intensity may also be a factor masking the endogenous rhythm in humans. Although the intensity of light found here to affect temperature was high, others have reported behavioral and physiological effects with much lower levels (e.g., Bojkowski et al., 1987; Boyce & Kennaway, 1987; Czeiler et al., 1989; McIntyre et al., 1989; Moore-Ede, Sulzman, Fuller, 1982; Sulzman, Fuller, & Moore-Ede, 1979). Thus, a prudent approach suggests that ambient light intensity be considered another possible factor

masking the endogenous temperature rhythm.

The findings reported by Moore-Ede, Sulzman and Fuller (1982) also relate to the present findings. They describe the tonic effects of light in squirrel monkeys on body temperature and activity. Light intensities of either 600 lux or 60 lux were contrasted with darkness. Whenever light was presented (either 600 or 60 lux) body temperature increased; when the light was removed, body temperature decreased. The effects were most noticeable during the subjective night. Under continuous light conditions a higher body temperature was maintained with 600 lux compared to 60 lux. Since a constant routine could not be used with monkeys, as used in the present study with humans, activity of the monkeys covaried with the light condition. Therefore, the authors concluded that activity was a major factor contributing to the corresponding increase in body temperature. Again, however, photic stimulation alone may have played a substantial role.

The findings have both theoretical and practical implications. Our data leave little doubt that nighttime ambient illuminance levels have a substantial effect on physiology and behavior. Others have also reported effects on humans of nighttime photic stimulation (Badia, Culpepper, Myers, Boecker, Harsh, 1990; Campbell & Dawson, 1990; French, Hannon, & Brainard, 1989). Thus, from a practical perspective, for those working out of phase with their circadian rhythms (e.g., shift work, etc.), bright light might be used to enhance alertness. The latter might result in substantial increases in productivity and in an important decline in costly accidents. However, before such implementation occurs, data concerning a "light intensity by alertness" function are needed to determine the most efficacious intensity levels. Further, more research addressing the critical physiological substrates underlying the BL effects is needed.

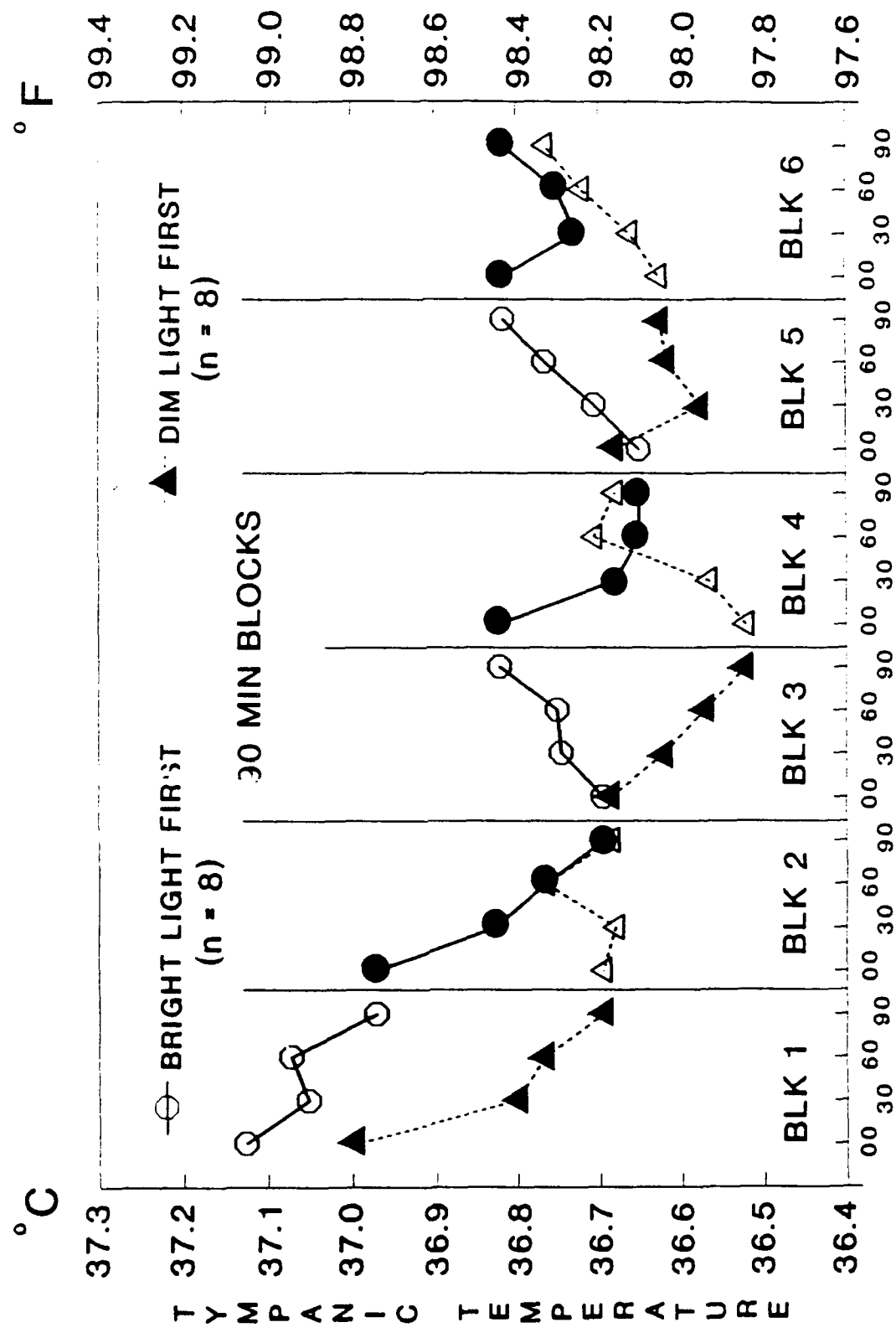


Figure 1 - Body Temperature and Bright/Dim Light

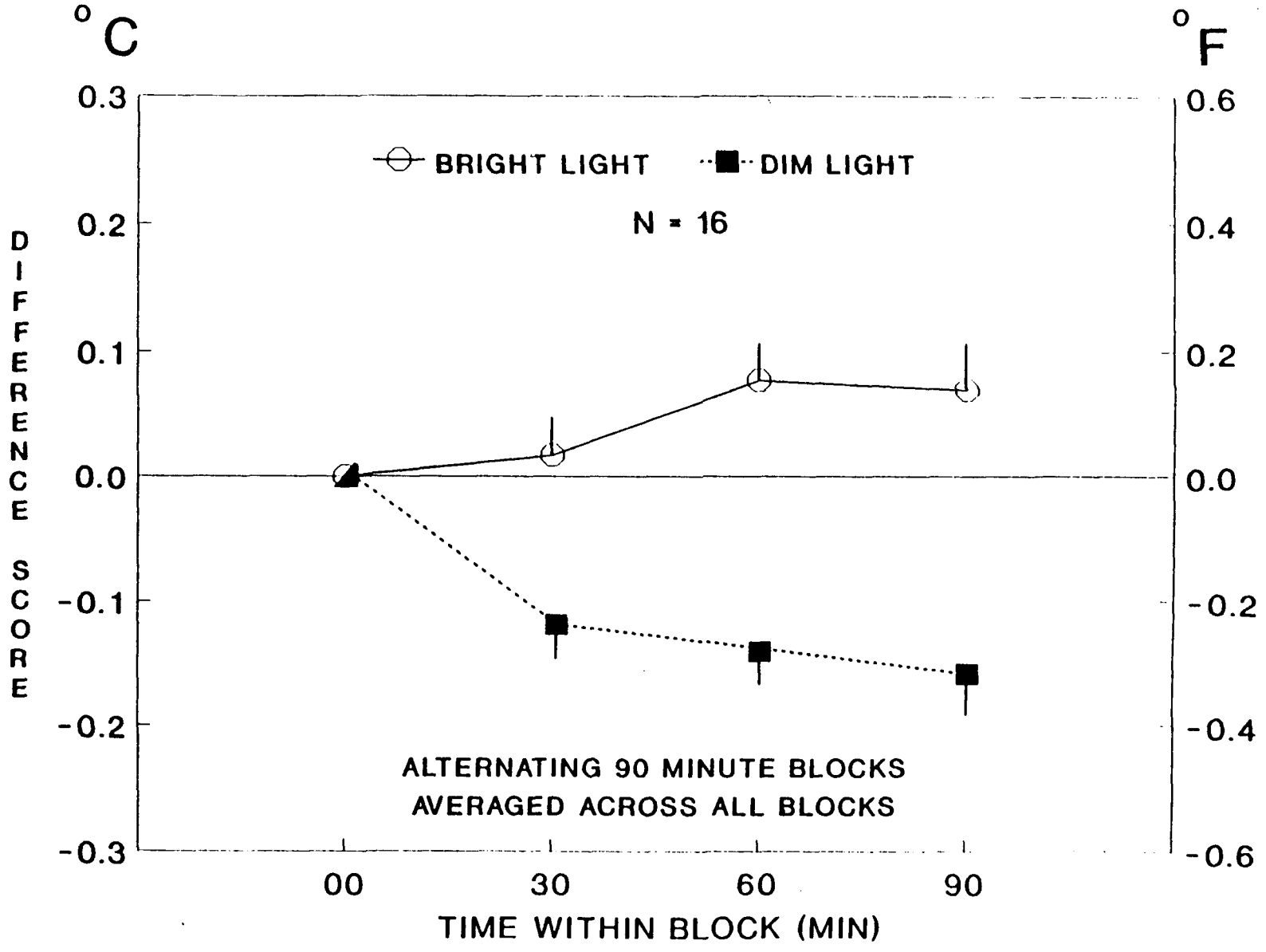


Figure 2 - Temperature Difference Scores and Bright/Dim Light

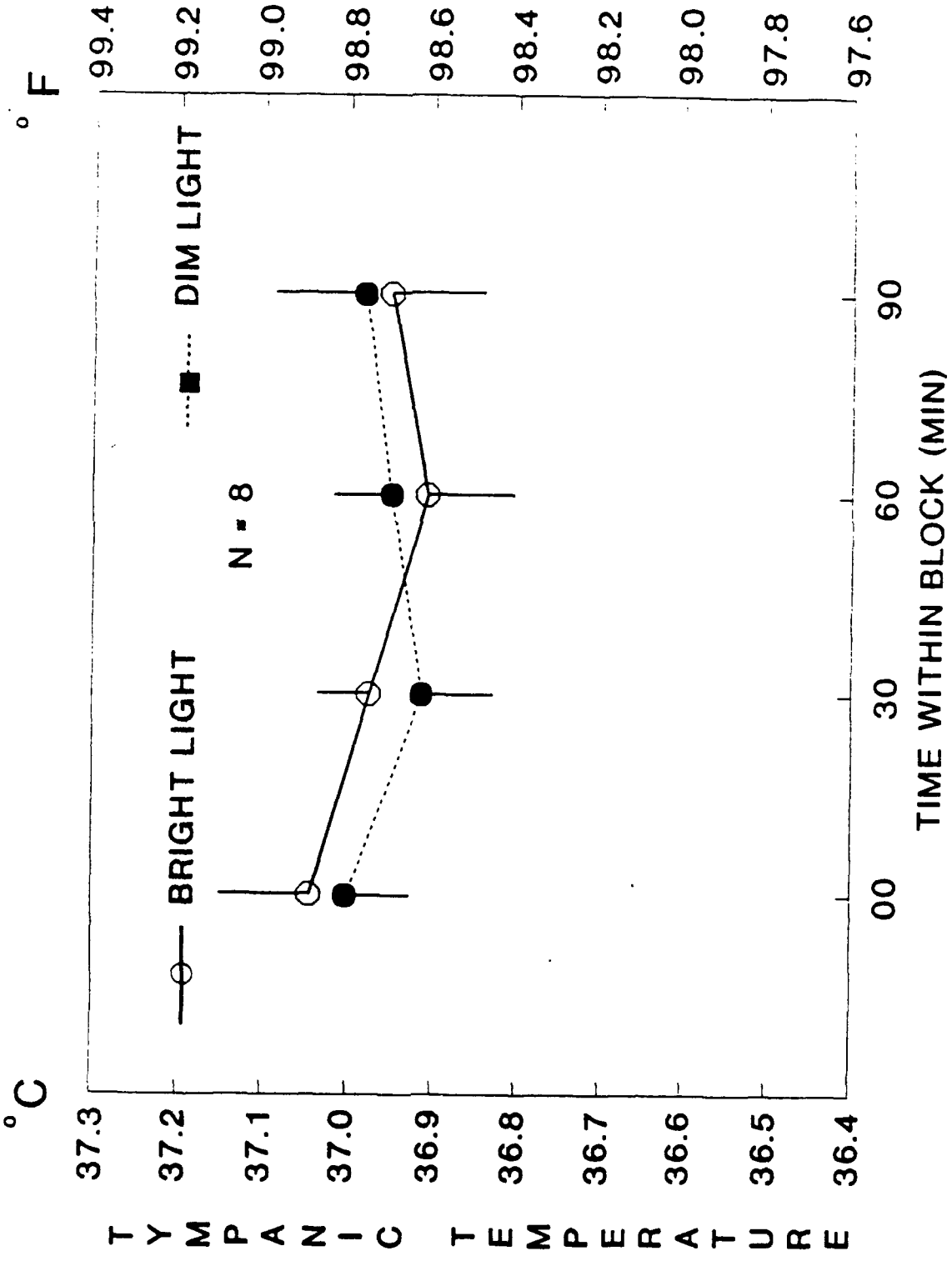


Figure 3 - Daytime Body Temperature

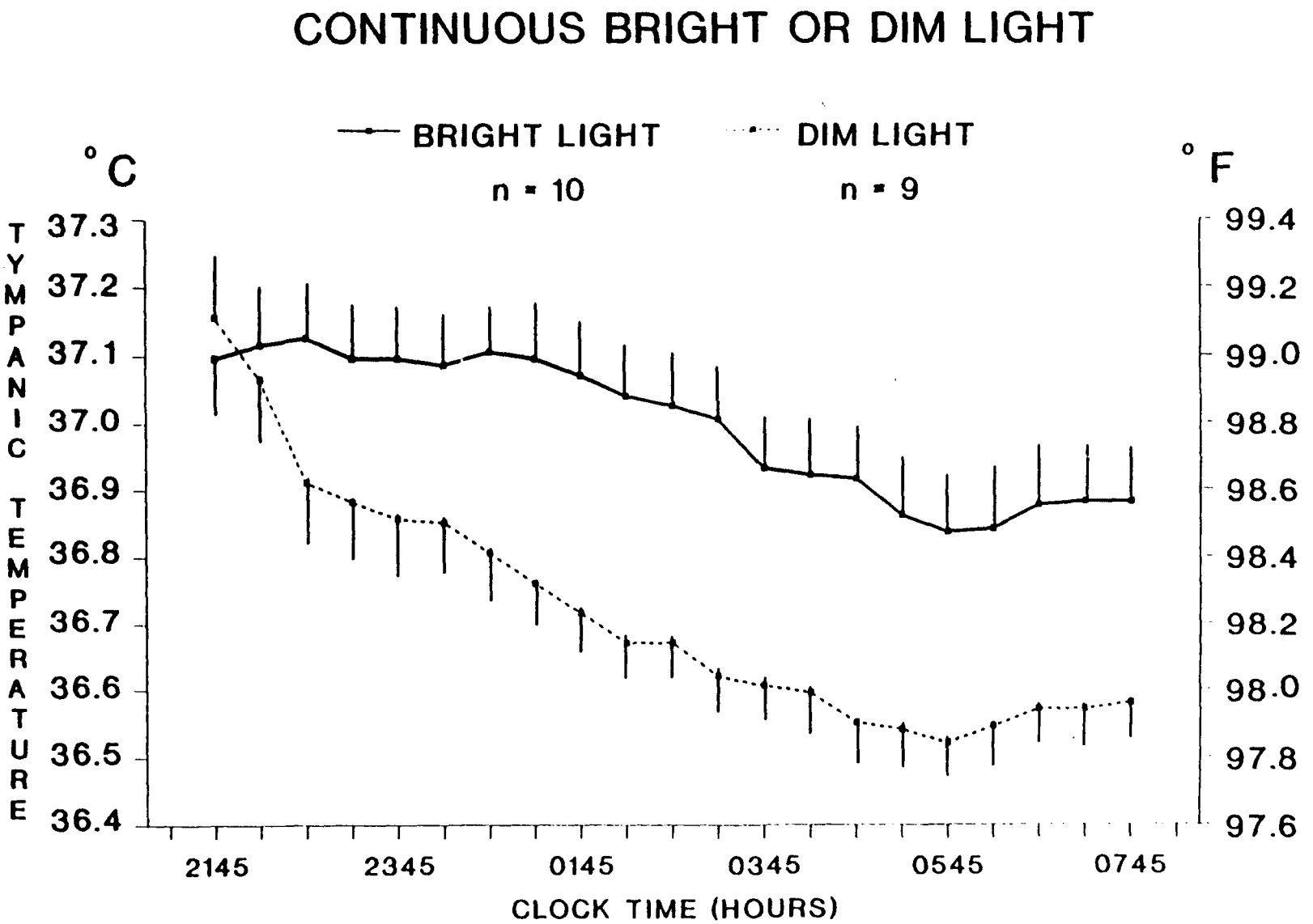
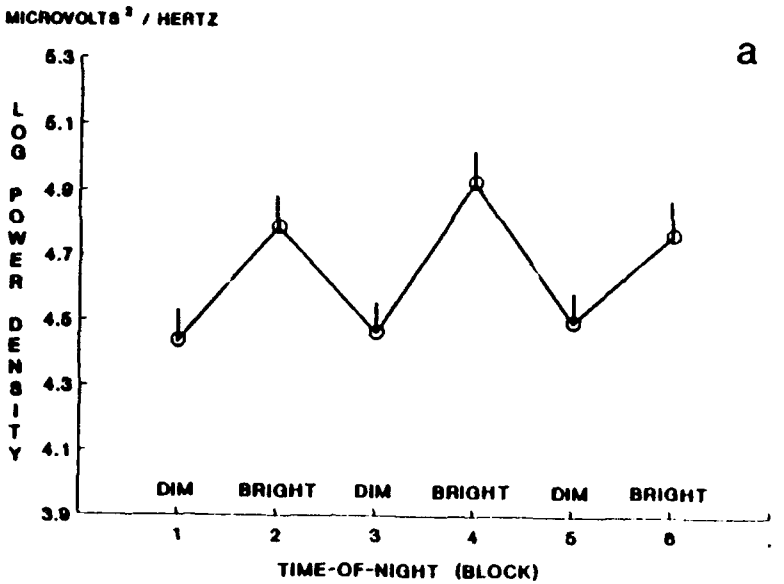


Figure 4 - Body Temperature Under Continuous Lux

BETA - Cz SITE

POWER DENSITY



DOMINANT FREQUENCY

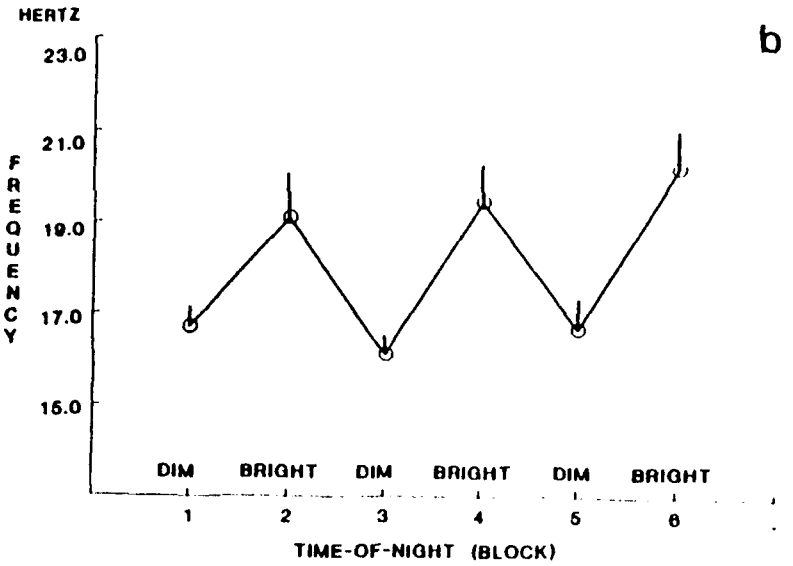


Figure 5 - Beta EEG

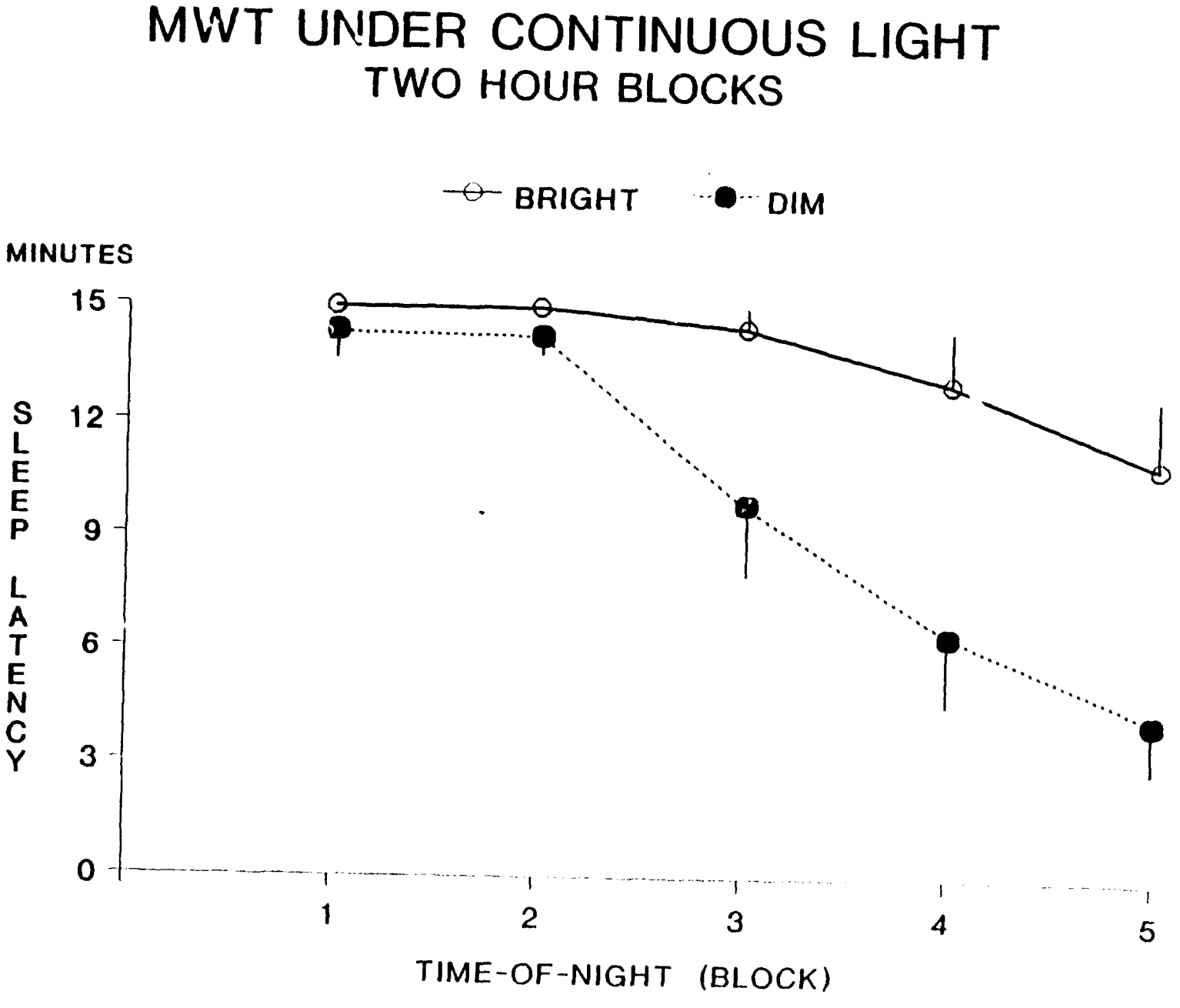


Figure 6 - Sleep latency scores from the Maintenance of Wakefulness Test

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7.0 CONCLUSIONS

Review of Progress

The research program was divided into three phases. The objectives of each phase are presented below along with a description of progress in relation to each objective.

PHASE 1 - DEVELOPMENT OF NEUROPHYSIOLOGICAL AND PERFORMANCE MEASURES

Objectives

* to develop furtner our ability to measure, analyze, and interpret characteristics of ERPs shown in our previous research to be correlated with performance during sleep deprivation;
* to explore characteristics of ERPs that have promise in relation to the objectives of the program;
* to develop our battery of performance measures to be able to specify which aspects of performance are related to ERPs.

Accomplishments

ERP MEASUREMENT AND ANALYSIS - During phase 1, hardware was acquired and software was developed to permit acquisition and analysis of event potentials and performance. Our software (called "EVAL") gives us the ability to acquire, measure, analyze, and display ERPs that exceeds that of most research laboratories. The following is a list of key features of EVAL.

*It was developed for a microcomputer and can be implemented (with minor modifications) in a variety of PC and workstation environments.
*It is written in "C" programming language which maximizes its portability.
*It includes a digital filter routine that can be used to filter either individual or averaged waveforms.
*It includes two artifact correction routines... one which rejects contaminated waveforms based on detection of voltage levels above a specifiable criterion and one which identifies and removes (using regression analysis) activity due to eye movement.
*It has the ability to display data on a sweep-by-sweep or averaged basis.
*It includes a peak-picking scoring routine (an area under the curve measure is being developed) that permits measurement on a sweep-by-sweep or averaged-waveform basis.

Importantly, the hardware/software arrangement was also designed to permit collection and measurement of ERP features that have not beer frequently studied and that show promise in relation to research objectives.

PERFORMANCE MEASUREMENT - We acquired several computer tasks including those in a recent version of the Performance Assessment Battery (Thorne et al., 1985) and tasks developed in our laboratories. We also developed an apparatus for the study of reaction time that 1) does not require that subjects be at a fixed test station, 2) does not require the subjects to consciously maintain a "response-ready" position and 3) requires

only minimal response effort. The apparatus consists of a small, light weight, "hand-shaped" wooden base to which is attached a photocell network. The subject's hand is strapped to the base so that the fingers are positioned under the photo beam. Only the forefinger is free to move. The task requires that subjects lift their forefinger to "break" the photobeam. The response board is attached to the recording apparatus with a length of cable that permits movement of the arm and hand freely when the subject is either sitting in a chair or in bed.

EXPERIMENTS COMPLETED - The general purpose of the studies completed in Phase I was to validate our measures, refine experimental procedures, address measurement and analysis issues, and evaluate the influence on ERPs of basic processes, such as habituation and conditioning.

Our initial efforts raised some important conceptual issues needing careful study. Experiments 1-3, and 5 were completed to further study unexpected decrements in the amplitude of ERP components under conditions of repeated testing. The objectives of our research program concerned understanding the effects of sleep deprivation and irregular sleep on ERPs and this objective required repeated testing under constant experimental conditions. Understanding deprivation-related effects required an understanding of ERP changes due to factors other than deprivation.

Each of the four experiments furthered our understanding of the important role of habituation in ERP variation. Experiment 1 suggested that changes in arousal level do not provide a sufficient explanation of P300 amplitude variation during an extended and "boring" test session and that attention may be the major factor. It may be important that variation in P300 amplitude was found even though accuracy of responding did not vary. The data suggested that the reductions in P300 amplitude during the simple RT task are associated with "readiness" to respond to rare or unexpected stimulus events. The results of Experiment 2 suggested that ERPs are components of an "orienting response" but are either more sensitive than peripheral measures of orienting or reflect other cognitive mechanisms. Experiment 3 provided considerable information about ERP changes during Pavlovian conditioning. Arousal again was explored as an explanatory factor. Variation of arousal may not be a sufficient condition for ERP variation but evidence was obtained to suggest that the cognitive processes reflected by P300 may be altered by increases in arousal associated with aversive events. The finding that the ERPs of the learners differed from those of nonlearners is a demonstration that ERPs are related to individual differences in performance.

PHASE II - EVOKED POTENTIALS AND MEASURES OF PERFORMANCE

Objective

* to demonstrate that evoked potential measures are sensitive to experimental conditions known to affect performance and are at least as sensitive as more conventional measures.

Accomplishments

We completed several Phase II studies. The objectives of each of the studies were entirely consistent with the above stated objective although the protocol of the studies was not exactly as described in the original proposal. Our decision to depart from the proposed protocol was based on the findings of experiments 1-4 and on recently published research from other laboratories.

In one series of studies we examined the effects of sleep loss as proposed, but added a photic stimulation factor. Our review of research on photic stimulation suggested that bright light should have some effect on performance during sleep deprivation. We reasoned that by testing sleep deprived subjects under bright and dim light, we would be able to assess the sensitivity of ERPs to the potent effects of sleep loss and at the same time to the more subtle (we believed) effects of bright light. To our surprise, the effects of bright light on our measures were not at all subtle and in fact, were quite powerful. Since these findings were, in relation to the existing literature, new and surprising and, in relation to the applied focus of our research, dramatic and exciting, several follow up studies were done.

In a second series of studies in Phase II, we investigated another factor that our own research and that of others suggested would have subtle effects on performance and would thus provide a good test of the sensitivity of ERP measures. In two experiments we examined time of day effects on ERPs and performance of nondeprived subjects. These studies also permitted us to study, on a subject-by-subject basis, the relationship between ERP variation and performance variation.

The experiments showed that ERPs are related to variations in performance. Finding ERP correlates of time-of-day and ultradian variation in performances 1) establishes the sensitivity of ERP measures, 2) provides information about the processes underlying such performance variation, and 3) suggests that ERPs might be useful as predictors of performance readiness. With regard to the latter, the relationship between behavior and the negative ERP potentials, N100 and N200, should receive special attention as they can be obtained with a procedure which does not require a response or even the attention of the subject. This would enable use of the measure with subjects who because of work demands, motivation levels, etc are unable or unwilling to devote attention to an experimental task.

PHASE III - ERP/PERFORMANCE RELATIONSHIPS DURING PROLONGED EXPOSURE TO STRESS

Objective

* to determine whether ERP measures predict deterioration in performance accompanying exposure to a high-demand work environment during prolonged sleep deprivation

Accomplishments

A protocol was developed for addressing issues related to Phase III objectives that did not require extensive sleep deprivation. We assessed the predictive relationship between ERPs and performance across levels of arousal ranging from

alertness to great sleepiness by study of the wake/sleep transition. Under the wake/sleep transition studies, sleep-deprived subjects were trained to perform a behavioral task while awake and sitting in a chair and then instructed to continue to perform the task as they went to sleep while lying in a bed. Thus, behavioral and ERP measures were obtained from subjects while they were alert and as they were overwhelmed by sleep.

Two lines of research suggest that the wake/sleep transition serves as a model for the study of behavioral and physiological changes associated with sleep loss. First, there are several studies suggesting that performance deterioration in sleep deprived subjects is accompanied by changes in EEG measures that are identical to those that occur during the wake/sleep transition. Second, studies of ERPs following sleep deprivation show ERP changes that are identical to the changes we have seen during the wake/sleep transition.

A significant advantage of the wake/sleep transition for the study of sleepiness, behavior, and ERPs is that it permits collection of meaningful amounts of data in short periods of time. Using this model, we completed three separate experiments exploring factors critical to understanding ERP changes. Time and resources provided by the contract would not have permitted addressing these factors using a 72-hr sleep deprivation protocol.

An additional important advantage of the wake/sleep transition model is that it provides data that facilitates interpretation of ERPs collected from sleepy subjects. Our existing data make it clear that ERPs collected during sleepiness resemble waveforms observed during sleep. By collecting data at all levels of wakefulness and sleep, the ERPs during the transition can be compared with those collected during wakefulness and those collected during sleep.

The wake/sleep transition protocol allowed us to address the objectives of this contract, i.e., it allowed us to determine 1) whether ERPs change systematically as a consequence of sleepiness and sleep onset; 2) whether ERP changes are correlated with performance changes; and 3) whether ERPs are correlated with individual differences in performance. Most importantly, the wake/sleep transition experiment allowed us to quickly and efficiently address some of the technical objectives of the contract such as 1) assessing the role of latency variability in reduced component amplitudes, 2) determining whether collecting ERPs from multiple sites more clearly describe neurophysiological changes, 3) establishing whether alternative means of data reduction such as principle component analysis provide a clearer description of the relationships, 5) exploring whether the findings obtained with auditory potentials generalize to other stimulus modalities, and 6) exploring whether the several measures of evoked potentials are selectively related to different aspects of performance (response speed, memory retrieval, etc.).

Significant Findings

ERP Studies The completed ERP studies 1) established the sensitivity of ERP measures to factors known to alter arousal, 2) provided information about the cognitive processes underlying performance variation, and 3) provided support for the notion that ERPs are useful as predictors of performance readiness.

We are most pleased with our progress in understanding the profound ERP changes associated with sleepiness and the relationship between these changes and performance. The most striking change was the gradual emergence of a negative potential at 300-400 ms following stimulus onset. We refer to this negativity as N_{350}. We found that the amplitude of N_{350} to be related to responding during lowered arousal and in some subjects the relationship is quite strong. Because of the close relationship between this waveform and performance, several experiments were initiated to identify its determinants and its relationship to cognitive processes such as stimulus detection, stimulus evaluation, response selection and emission, and memory processes. Our research established that N_{350} is related to psychological processes. That is, the amplitude of the deflection is dependent on the instructions given to the subjects and occurs with an omitted stimulus procedure (subjects are instructed to respond when an irregularly occurring stimulus is omitted). Its amplitude varies with the sequencing and probability of stimulus presentations suggesting a relationship to what has been called "automatic" processing. Its amplitude also varies, however, with the task relevance of the eliciting stimulus which suggests a relationship to "controlled" or conscious processing. Further study of this waveform should provide greater understanding of the cognitive changes associated with sleepiness and should also provide a means of monitoring changes in performance readiness due to reduced arousal.

We also observed that during alert wakefulness and during sleep, ERPs to task-relevant stimuli are comparable in shape along the midline (i.e., at Fz, Cz, and Pz). During the wake/sleep transition, however, the shapes of the ERPs at the different recording sites differ and sometimes quite markedly so. During the early stages of the transition (when subjects are still reliably making finger-lift responses), ERPs recorded at the parietal electrode are unchanged in shape. At the frontal and central electrode sites, however, the shape of the recorded ERPs have begun to change. Thus, morphological dissimilarity of ERPs along the midline identify a period of transition from alertness to sleep. We believe this process has implications in relation to arousal-related changes in cognitive processes and performance.

Bright Light Studies Subjects under the nighttime, bright-light condition had higher body temperatures, lower melatonin levels, were more alert, less sleepy, and performed better than subjects under lower levels of illumination. These findings have important implications for all nighttime situations where alertness and high performance levels must be maintained. This

would be especially the case for individuals working out-of-phase with the normal day. It would also be of great benefit to those who work shiftwork schedules where the work load requires alert monitoring. In particular, our data suggest that those working in the field under sleep deprivation conditions may benefit greatly by exposure to bright-light conditions. Additionally, since melatonin may be importantly related to the energizing effect of bright light and since melatonin can be altered by means other than bright light, it may be possible to induce the energizing effect of photic stimulation using other means (for ex. drugs). We believe these findings to be of great significance and deserving of further study.

In sum, the completed experiments brought us close to our contract goals of 1) gaining a more complete understanding of the effects of sleepiness and sleep loss on evoked-potential components and their relationship with performance and 2) showing that a neurophysiological test based on ERP measures can be used a) to predict changes in performance resulting from sleepiness and sleep loss and b) to distinguish between those individuals who will perform well and those who will perform poorly.